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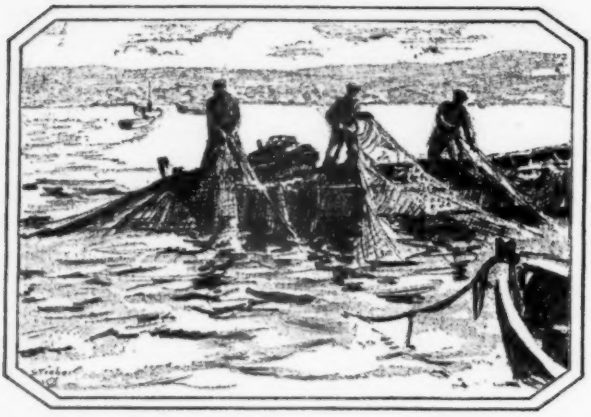

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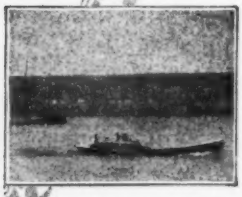

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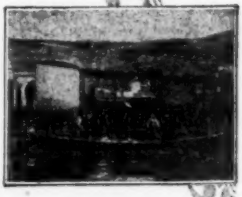

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MARCELLO MALPIGHI

UNIV. OF MICH.

MARCELLO MALPIGHI

Bolognese Physician and Philosopher[1]

JOSEPH FRANCHINI, M.D.

Professor of Tropical Medicine in the University of Bologna.

Marcello Malpighi lived during the seventeenth century at a time when science was carrying on a strenuous fight against the ignorance of the classes and when innovators were being rewarded by tortures such as were inflicted upon Galileo, to whom we owe the introduction of the experimental method of the physical sciences.

It was a time when in this place and in that place there shone the cruel lights of the pyres which turned to ashes the bodies of many true and earnest men among whom Michele Servetus and Giordano Bruno stand out conspicuously. The lonely voice of the illustrious seer was burdened with the task of destroying the enormous amount of fictitious reasoning accumulated by the pedagogues then reigning in the schools and among the people at large. At that time the Arabs and Galenists were revered as the rulers of medical science at Messina. At Bologna, at Padua and at Rome, medical charlatans, crushed under the weight of the interpretation of the Bible, were fighting for dogma against reason. To raise the torch of truth amid such surroundings did not disturb or excite the masses, but the learned were aroused to fight on the one or the other side. The odious persecutions which his contemporaries inflicted upon Malpighi need not surprise us when we realize that about the same time Bellini was stoned by the students of Pisa who refused to tolerate his lessons in practical anatomy; and that in Paris the professors were prevented from lecturing by having straw and hay thrown at them and were forced to obtain the permission of the students before they were allowed to retreat in safety.

Lessons in practical anatomy were given in private houses with por-

[1]Lecture delivered before a joint meeting of the Johns Hopkins Hospital Historical Society and the Johns Hopkins Medical Society on November 1st, 1928.

tions of bodies stolen during funerals or from houses, or dug up at night time from cemeteries, the doctors running the risk of being attacked by monks who were guarding them, or by dogs and vultures when they seized the bodies of criminals who had been executed. The latter mishap, it is said, overtook Vesalio, and Hyrtl confirms the statement that, at the beginning of the 15th century anatomists were hated so much that they had to take refuge in grottoes. It can readily be understood, then, that Malpighi found anatomy full of errors, although it had been advanced by the work of Eustachio, who was the first to introduce the art of dissecting bodies, by the work of Berengario, Carpi, Vesaglio, Fallopio, Valsalva, Ingrassia, Varolio and many others.

Claudio Galeno of Bergamo had attempted to explain the functions of the viscera and the causes of pains, but without rendering the subject clear, since he paid more attention to dialectics than to exact observation. Hence we are not surprised that the world of science was agitated by the bitter disputes between dogmatists, empiricists, methodists and pneumatists, the only acute observers being Rufo, Sorano, Areteo, Celio, Aureliano and Celso. Besides this, there was the influence of the Arabs who, being devoted to Galeno, imposed upon all, for seven centuries, the love of the miraculous, although they made contributions to progress through the introduction of universal chemistry and the differentiation of mineral waters, of various medical preparations and the description of several diseases. But their disciples were superficial and fanatical; they busied themselves with dialectics more than with observations from real life. And even when they laid aside philosophical discussions, they merely guessed at the cause, believing in spontaneous generation rather than trying to prove it with facts and experiments: "All the material," says Atti, "that Malpighi found and gathered together consisted of contentions about medical terms, strange imaginary fancies, pretexts, mistaken opinions and disgraceful deceptions."

At Montecassino first sprang up the Academy of the New Art, in which the doctrines of the Arabs were beginning to be abandoned. Mondini (or Remondini) reconstructed anatomy in Bologna, which, in the hands of Malpighi, afterwards reached a very high level, becoming the light of science and being rendered still more fruitful by the discovery of the microscope.

Princes and patrons of the *belles-lettres* sometimes rendered aid to research workers, and among these the following must be remembered: Viscount Ruffo of Francavilla, who showed great hospitality to Malpighi at Messina; the Grand Duke of Tuscany, Ferdinand II, and his brother, Leopold, who founded the Academy of Experiments with Francesco Redi, Torricelli, Borelli and others. These men, convinced of the importance of anatomy to mankind, attended the experiments and welcomed physicians to their homes. Nor must we forget Christina of Sweden, the wife of Gustave Adolphus, who gave up her throne in order to be able to live in Italy and encourage literature and science.

The Bolognese antagonists showed bitter hatreds, intrigues and petty jealousies, an example of which can be seen in the treatment of Malpighi by his colleagues: For instance, Sbaragli, who although himself something of a progressive worker in medical science, a lecturer on medicine and anatomy, joined Mini in carrying out secret acts of vandalism and destruction in Malpighi's study. Without respect or pity for the aged scientist, they broke the microscopes and destroyed the manuscripts that had been saved from a previous and perhaps malicious fire in his town house. Nor was this same Sbaragli less scrupulous in dealing with questions as to boundary rights between his estate and that of his neighbor; and it was he who, to spite Malpighi, obliged the students when they obtained their degrees to swear that they would defend the doctrines of Aristotle, Galeno and Hippocrates. Also, Dr. Cucchi, Professor of Medicine, influenced by a publication by Montalbano, incited the students against Malpighi, so that they even threatened to kill him. There were others, too, who treated the posthumous works of Malpighi, the great scientist, with scorn. Malpighi, who was consistently of a prudent and kindly nature, always met these insults and injuries with silence and magnanimity, an attitude that was perhaps more exasperating than brutal fighting in those days when the sword and the dagger were the usual means of defence and when the streets were daily stained with the blood of men murdered for revenge. Indeed, Sbaragli's brother was killed by Malpighi's brother.

Nor could all antipathy to this great man be averted even by his removal to another city. In Bologna his slanderers condemned the

study of comparative anatomy and biology, superciliously regarding his microscopic experiments as "inutiles et libidinosi ingenii abortus." Even in the city of Messina itself to which Malpighi had been welcomed with special honors, his discoveries and a new healing method, which was not quackery, served to arouse against him, under the instigation of Lipari and Avellini and, in spite of his admirers and protectors, the whole Academic Senate, who invited him to a public confutation. This insulting invitation Malpighi very rightly refused, and at the same time resigned from the chair he was holding, together with the honors and riches associated with it, and left the city which, because of its nearness to the sea, offered him abundant material for study.

But during these four years in Messina, Malpighi had an opportunity to study the anatomy of fishes, the anatomy of the brain, which resulted in his discovery of the nature of the grey and white matter and of its relation to the spinal cord, the sense of touch, the structure of the viscera, of the tongue and the sense of taste, of the kidneys and the urine, the fat, the omentum, the spleen and the physiological anatomy of plants, in which he made out the airducts or tracheae and their cells. In the same city he began what promised to be an extensive treatise on Italian anatomy which was meant to record and do honor to the contributions of his fellow-countrymen to this science. This work, however, did not get beyond the description of the heart, because his friends, Borelli and Fracassati, would not allow his genius to dissipate itself in a mere work of compilation.

It is pleasant to remember that the religious spirit did not exert a bad influence and gave no support to his slanderers, for we note that Cardinal Negroni, in Bologna, stood up in defence of Malpighi and bade Mini stop his injurious campaigning; that Canon Trionfetti destroyed in Rome the libels printed by his own brother Giovan Battista and that Pope Innocent XII appointed Malpighi his body physician and was much grieved at his early death.

While Malpighi was still alive, the people of Bologna erected a monument to him in the Archiginnasio, the older building of the university, and one feels a kind of relief in reading the names of his numerous admirers and supporters; in Bologna, Massari and Mariani (his teachers), Bonfiglioii, Fracassati, in Pisa and elsewhere the Ne-

apolitan anatomist and mathematician Alfonso Borelli; then Bellini and Redi; in Rome, Lancisi, Baglivi, Pope Innocent XII, of whom Malpighi speaks in his memoirs with touching tenderness. Malpighi married Massari's sister, Francesca, thus strengthening the ties of friendship that bound him to his master. To her he was a devoted companion, and her death a few days before his own undoubtedly hastened his own end. From Mariani he took the system of cures "quae summo cum judicio et felicitate ab eo absolvebantur," a system that in the direct Autobiographia of the Royal Society of England is described as "verus tutiorque medendi methodus" (a true and more salutary method of healing).

Malpighi declared himself indebted to Borelli for any advance he had made in experimental philosophy, and the friendship between the two men was altogether touching. Borelli was the friend, the confidant, the guide, the adviser. For a long time there was no discovery made, no observation, no complaint from Malpighi, of which Borelli was not first informed by letters full of scientific content and manifestations of tenderness and reverence.

In Borelli's house in Pisa he practised anatomical dissections and researches, among which is that famous one on the spiral fibres of the heart. Credit for the discovery, however, later on was contested by Borelli himself who claimed it as his own.

Many well-known authors have written sketches of Marcello Malpighi's life. He was born at Crevacuore near Bologna on the 10th of March, 1628, two years after the birth of his friend and rival, Francesco Redi. His parents were honest land-owners. At twelve years of age he began to study Latin, and at seventeen he came to Bologna where Francesco Natali took charge of his mental and moral education and initiated him into the study of medicine. When twenty-one years of age he was left an orphan and passed under the tutorship of Bartolomeus Massari, Professor of Anatomy, who had instituted in his own house a society called the *Coro Anatomico*, with the idea of continuing the studies on the circulation of the blood, recently discovered by Colombo and Cesalpino. Harvey himself declared that among Malpighi's discoveries were the reservoir of the chyle and the thoracic duct. There were daily discussions, and Malpighi, who was then twenty-two, was received into the Society as the first member of the

Coro Anatomico. A year after Marcello's marriage with Francesca her brother, Massari, died and the *Coro* was continued by Mariani on the same basis as the peripathetic medicine according to the teaching of Hoffmann, Cesalpino, Buonamico, Cremonini, with practical lessons on human bodies and animals. This irritated the Aristotelians, the empirics, and the followers of the medical schooling of the Arabs who could not tolerate the doctrines of Hippocrates, with the result that Malpighi was opposed in every possible way at his examinations for the doctorate. However, at twenty-eight we find him teaching publicly at the University of Bologna, and soon after, at the request of the Grand Duke Ferdinand II, at Pisa where he held the chair of theoretical medicine for three years. He became one of Borelli's best friends, and began that scientific work which afterwards brought him to the summit of his glory. To defend the progress of science, he wrote certain dialogues containing an imaginary discussion between a Galenist and an Iatromechanist, into which, opportunely, a third person entered who did not belong to any sect and could, therefore, express an unbiassed judgment. These dialogues were destroyed in the fire that occurred in his country house. At Pisa he made the discovery of the spiral structure of the fibres of the heart and the interstitial structure of the testicle. Because of these researches the Grand Duke decided to protect the experiments of the physicians and to found the *Academy of Experiments*. Harassed by the animosities of Sbaragli, he abandoned the chair at Pisa and returned to Bologna where he resumed his studies and discovered the texture of the lungs and the mechanism of respiration. In all this work we was persistently opposed by everybody, even by his friends Fracassati and Borelli. Truston and Willis, both Englishmen, however, intervened in his defence.

About this time he wrote a treatise on the organic liquids, the nature of the blood and its alternate transformation into red and black, on purgatives, nourishment, gastric juices, saliva and the fever of Pisa. He was always indefatigable and of prodigious activity. One day at Crevacuore, where he had gone for private business, having found a fish, he discovered the circulation of the blood in the gills. This episode recalls the story of Pasteur who, when visiting at Fabre's house, was shown a cocoon which he had never seen before, which

led him to discover the cause of the disease of the silkworm. On the death of Mariani, Malpighi, who was then thirty-four years old, was requested by the Senate of Messina to go there as Professor of Medicine. He held the chair for four years, until disgusted by the petty disputes of his colleagues he decided to return to Bologna, despite the insistence of the senators. This was one of the most active periods of his scientific career. At Bologna he took up his researches once more and excelled also in clinical work. He studied the structure of conglobated glands and the uterus, and compiled that admirable work which was afterwards so lauded by Boerhaave. He worked for a long time on the structure of the heart (*De polypo cordis*) and on bones, and made an extensive study of a petrified skull, a mould in plaster of which is still on view in the Anatomical Museum of the University of Modena, the original being in the Museum of Prague. Malpighi also made a study of corns, of the nodules in gout and of the teeth.

Exhausted by research, he went to Padua where he was surprised to find the Professor of Anatomy so far behind in medical science as to believe, among other things, that the muscles of the thorax existed simply to fill the spaces between the ribs.

It was natural that his discoveries should arouse almost universal admiration and cause a wide-spread commotion in the whole of Europe. The Royal Academy of London asked him for information, and Malpighi, in a very short time, was able to give a complete report of the genesis of the silkworm (*dissertatio epistolica de bombyce*), which when sent to London brought him, through the influence of Oldenburg, the honor of membership in the Academy. Eternod placed him in the ranks of those men whose beliefs, reaching far into the future, would be shared two or three hundred years later by the whole world; and his prophecy was fully verified, since after him one must come down to Fabre before being able to find biological observations as precise as those of Malpighi.

This work was followed a year later by the treatise 'On the Anatomy of Plants' which reached London at the same time as that of Grew, and by another one, 'On the development of the chick in the egg and on the incubation of the egg,' from which Malpighi was hoping to obtain great help toward the revelation of the mysteries of anatomy. This led to a stimulating controversy with Bellini, Redi and Olden-

burg, which, however, was not capable of repressing his versatile genius. He then investigated the ear, examined an eagle and together with Redi made a study of certain worms existing in the liver of man, of oxen, of wormy swine and of the porcupine. He studied the tapeworm, the glow-worm, butterflies and the fecundity of women. He described a vessel winding through the tubes of the uterus and the evolution of the uterine horns. Haeckel, who looked upon Malpighi with the eyes of a naturalist and philosopher, rightly declares that only Lamarck and Wolf, in 1700, and Darwin and Mueller, in 1800, are worthy of being placed in the same rank with him.

Although a victim of the famous fire that brought sorrow to all scholars and especially to his friend and admirer Redi, he started work again with increased zeal, retrieved the lost microscopes and wrote, to satisfy the curiosity of the scholar Maserio, a treatise on the generation of metals. This work, although consisting of only a few pages and simply demonstrating the versatility of his brain and his acuity of observation, no longer arouses astonishment as one becomes accustomed to seeing this great man forging far ahead of his age. He reviewed with ease almost all branches of science, including anatomy, philosophy, pathology, histology, botany, zoology, biology, mineralogy, archeology and the fine arts, examples of which he collected in his house in a small museum. In every one of his observations there is evident the genius which understands clearly everything that it sees and goes straight to its aim. He paid no attention to the ridiculous disputations based upon paradoxes, nor did he waste time in useless scholastic argument or sectarian and aesthetic euphemisms.

As an eclectic forerunner in biology he stands forth as a mighty figure of a man who, during his too short life was an example of a diligent student of nature, a model of prudence, magnanimity and modesty in an environment often hostile, rarely appreciative of his work. Jeered at and menaced, we see him patiently taking up his work again, with charity to all. When a libel requires an answer, this comes out clearly and quietly from the pen of the master who shows himself superior to his century. He is one of those figures that every now and again appears to illuminate generations, indicating to the world a new road that they alone are capable of seeing. Strasburger speaks of him as "one of those few and solitary men whom progress rarely

offers us, a man without predecessors and without successors, for a hundred and twenty years passed by before one could notice any visible progress in vegetal anatomy." According to Nichet, he is the first of histologists; Koelliker calls him the first microscopist of modern times. If his writings had not for about two centuries fallen into such an unjust oblivion, we should see the name of Malpighi connected not only with a few glomeruli and strata, but with a great number of tissues and functions which he really discovered and described. In 1672 he sent to the Royal Society of London that admirable work *"Congesta historiola"* a document exhibiting science and foresight, and from which he himself expected to add greatly to philosophical and anatomical knowledge. And he was so sure of the truth of his own observations that he would not consent to the printing of his celebrated work *"De motu animalium"* for fear that others would appropriate the discovery for themselves. With confidence in himself he passed from the respiration of the lizard to the circulation and the respiration of the frog; he studied the anatomy of the camel, mineralogy, crystals, mushrooms, the nature of the hair, the human embryo in the uterus, the facial glands, the penis, the saliva, the tongue, the mesenteric veins and the lymphatic vessels of the sebaceous glands. He points out the way by study medicine, describes a tumor as big as a hen's egg suspended by a ligament in a woman's body and an ossified foetus in the womb of the mother. His publications are so numerous and varied that a whole volume would be needed to catalogue them all. A chronological index was published by Gaetano Atti who, searching at Crevacuore in Dr. Rigozzi's house, was lucky enough to discover in 1830 so many manuscripts as to be able to compile sixteen thick volumes that are still to be found in the University Library of Bologna. These are the writings which Malpighi himself delivered to his disciple Albertini, and which were bequeathed by the latter as a legacy to the Rigozzi family. It appears that some manuscript has been found glued to the scenery of the Communal Theatre of Crevacuore. Other works of Malpighi were found later on by Gaddi in the secret Diplomatic Archives of the Extense Court at Modena where is also to be seen the plaster mould of the famous human skull with which Malpighi studied the anatomy of the head. Still other manuscripts are in the University Library of Bologna,

in the Archiepiscopal and Communal Libraries; others are in the Lancisiana Library of Rome where the letters of medical consultation are to be seen, and some in the Vatican Library and Archives; some are in London and perhaps even in Bastia in the island of Corsica. Still others are in the hands of private individuals. How many more should we possess had not ignorance devastation, carelessness, fire and hatred not played havoc with his works!

But now the end approaches: Summoned to Rome by Pope Innocent XII to receive the title of body physician, Malpighi arrived there tired and ill. But his assiduity knew no limit, and many botanical, zoological and clinical observations belong to this period.

From the frequent pain in his head, from which he was suffering, he foretold the apoplectic stroke from which he suffered later. He used to tell his friends that death would take him by surprise, dressed and shod. As a matter of fact, in the afternoon of the 25th of July, 1694, a cerebral hemorrhage paralyzed his right side. Affectionately taken care of by Lancisi and Baglivi, he recovered partially, but only to suffer the deep sorrow of losing the beloved companion of his life, his wife, Francesca. His days were numbered; he felt the end approaching, and with a clear mind that surprised everybody he put his papers in order, pointed out the errors and corrections and entrusted them to his nephew so that he could forward them to the secretaries of the Royal Society of London, begging them to "accept this small thing and keep privately in memory of the great and singular privilege that I always had from them." The day after he had dictated this order, a second apoplectic stroke killed him at the age of 66, in the Quirinal Palace on the 29th of November, 1694.

Malpighi was a member of the Roman Arcadias and went by the name of "Terone Filaci." To Baglivi, helped by Lancisi, fell the sorrowful task of dissecting his body. His body was taken to Bologna.

Far from conciliating his enemies, his death rekindled the disputes and in these Sbaragli again was prominent. But Malpighi's "*Oculorum et mentis vigiliae*," then published at the expense of the British Society, put a stop to the envious campaign of defamation. The cycle is honorably closed by the printing of his "*Consultationes Medicales*," which Lancisi, Albertini and Vallisnieri attended to with scientific passion and devotion.

And now, in conclusion, I bow my head before this man, worthy of his country and of science, to whom the world today gratefully pays its debt of gratitude.

AN ACCOUNT OF THE ILLNESS AND AUTOPSY ON THE BODY OF MARCELLUS MALPIGHI, PONTIFICAL CHIEF PHYSICIAN (TAKEN FROM BALIVI'S BOOK)

Having been intimately acquainted for quite a long time with Dr. Malpighi in Bologna and having attended him during his mortal illness at Rome, it may be acceptable to the learned that I explain the history of the illness of such an illustrious anatomist and physician and the result of my dissection of his body.

Marcello Malpighi lived until the age of 66 years, had a tendency to thinness, was of medium size and height, for from his years of early manhood, he was subject to vomits, to bilious secretions, and having got rid of these troubles, he was a victim of acid vomits, of heart palpitations, of stones in the kidneys, of bloody urine and was also afflicted by slight gout.

Finally, weakened by these maladies, after his arrival in Rome, besides the heart palpitations, stones in the kidneys, and many most dangerous perspirations at night, as a result of previous troubles of body and mind, he was struck by apoplexy about mid-day on the 25th of July 1694.

Paralysis followed apoplexy, and the right side of his body was paralyzed, his mouth and also his right eye being affected.

We administered at once various remedies, *viz.:* injection of blood into the left arm but not into the paralytic arm as I generally did, because on Malpighi's body I could not adopt this treatment on account of the many different opinions of the doctors in charge. Cupping glasses were applied to the two scapulae, Cornaco's powder, mustard poultices to the soles of his feet, and many other remedies for headache and apoplexies. After 40 days of terrible pains, deliriums, faintings and other troubles, he became free from apoplexy, from the above mentioned paralysis, and from every other complaint.

But his maladies increased later. The illustrious doctor, owing to his previous illnesses, suffered from loss of memory and brain lesions on account of which at the slightest excitation he would burst out into

tears. He lost his appetite and suffered from tremors of the muscles and slight dizziness. Affected meantime by these and other syncopes, in the morning of the 29th of November of the same year, after the application of the venoma he was again struck by apoplexy. At last, terrible dizziness, most painful stones in the bladder which lasted about 8 days, loss of appetite and other more serious symptoms, brought about another apoplectic stroke which was the most violent of all, and in fact, after all kinds of remedies had been tried in vain, he died four hours after the stroke.

Dissection of Malpighi's body

After opening the body, I observed that the left side of the lung was rather flabby and especially livid in the posterior part that adheres to the back.

The heart had increased in size, the cavity of the left ventricle reached the thickness of two fingers' width; the bile was very dark in the gall-bladder. The left kidney was found in its natural state; the right one, on the contrary, was about half the size of the left one and the renal pelvis had dilated so much that one could easily put two fingers in it. Because of the width of the pelvis perhaps it happened that the stones produced in the kidneys descended at once into the bladder and came out, as I was often told, during his lifetime.

In the urinary bladder, there was a small stone that in the four days preceding the last stroke of apoplexy had descended into it, and in coming down had produced the last dizziness.

The other viscera were found to be in splendid condition. Having then opened the skull, we found in the cavity of the right ventricle of the brain about two pounds of clotted black blood; this hemorrhage had induced the apoplexy which caused his death.

In the left ventricle we found yellowish water weighing six ounces and containing a small quantity of tiny grains. The blood vessels of the brain were everywhere varicosed. Everywhere the dura was strongly adherent to the skull, contrary to the rule: this is all that, in the dissection of Malpighi's body, I could observe, in Rome, in the church of St. Vincent and Anastasius near the Quirinal, on the 1st of December, 1694.

THE BACTERICIDAL ACTION OF ROENTGEN RAYS[1,2]

HIRSH W. SULKOWITCH

Reider (1) was the first to observe the bactericidal action of x-rays. However, several experimenters, among whom were Berton (3), Minck (4), Whittlin (5), Blaise and Lambuc (6), Bergonie and Mongour (7), Musham (8), Schiff (9), and Levy-Dorn (10) failed to confirm his results. The study of this phenomenon was closed for a quarter of a century with the work of Zeit (2), whose work may be summarized by the last conclusion in his paper. "Roentgen rays have no direct bactericidal properties. The clinical results must be explained by other factors, possibly the production of ozone, hypochlorous acid, extensive necrosis of the deeper layers of the skin and phagocytosis."

This work was undertaken in connection with the study of the bactericidal action of ultra-violet radiation. There seemed to be adequate reason to believe that a germicidal effect with x-rays could be obtained, since the bactericidal effect has been shown to be continuous from the wave-length 3650 Å to the wave-length 1250 Å in the extreme ultra-violet, and that the germicidal effect increases with decreasing wave-length. This would be expected provided there were no points of resonance between the ultra-violet and the x-ray region.

EXPERIMENTAL PROCEDURE

The apparatus used in the roentgen-ray work was an x-ray diffraction apparatus built by the General Electric Company, and equipped with a Coolidge water-cooled molybdenum target, diffraction type x-ray tube, operating at an effective voltage between 35,000 and 40,000 volts, and a current of 20 milliamperes. A circular alloy casing surrounds the x-ray tube and contains fifteen apertures to which

[1] From a thesis presented to the Faculty of the Massachusetts Institute of Technology, Cambridge, Massachusetts, entitled The Bactericidal Action of Radiation. Part I. Ultra-Violet Studies. Part II. X-Ray and Cathode Ray Studies.

[2] Received for publication December 27, 1928.

diffraction cassets may be attached. The distance from the target to the aperture is 17.5 cm.

Standard 25 by 77 mm. microscope slides were cut in two, and after sterilization a thin layer of nutrient agar about 2 to 3 mm. thick was applied. The slides were then introduced into a covered, sterile

TABLE I

The effect of roentgen rays on bacteria

ORGANISM	DURATION OF EXPOSURE	EFFECT	
		Experiment 1	Experiment 2
	minutes		
E. coli	15	No effect	No effect
	30	About ½ original number of colonies	About ½ original number of colonies
	60	Almost all killed	Almost all killed
	120	All killed	All killed
Staphylococcus aureus	15	No effect	No effect
	30	No effect	No effect
	60	About ½ original number of colonies	About ½ original number of colonies
	120	A few colonies remained	All killed
Serratia marcescens (*B. prodigiosus*)	15	Slight inhibition	Slight inhibition
	30	All killed	All but a few killed
	60	All killed	All killed
	120	All killed	All killed
Pseudomonas aeruginosa (*B. pyocyaneus*)	15	Very few colonies	All killed
	30	All killed	All killed
	60	All killed	All killed
Sarcina lutea	15		None killed
	30		None killed
	60		Few killed

petri dish and the agar allowed to solidify. A strip of agar about 3 to 4 mm. wide was then cut off with a hot sterile needle in order that the edge of the agar might not have contact with the frame of the apertures in the casing. Because of the presence of a fan inside the casing, used in cooling the tube, it was necessary to place sterile paper in front of each aperture to prevent any dust from reaching the agar

plate. The standard cultures used in this research were made by the transfer of one standard loop[3] of culture to 10 cc. of nutrient broth and incubated at 37.5°C. for twenty-four hours. Dilutions were made by transferring six 4 mm. loopfuls of the standard culture to 10 cc. of nutrient broth. The nutrient agar-coated slides were then inoculated by smearing the surface of the medium with two 4 mm. loopfuls of this dilution. Owing to the scanty growth of *Sarcina lutea* it was found necessary to inoculate this organism by removing two 4 mm. loopfuls from the standard culture directly, instead of using the dilution as described above.

After inoculation, the slides were set into the apertures of the casing and exposed for a definite length of time, and then incubated at the optimal temperature of each organism for twenty-four hours, and in the case of *Sarcina lutea* for forty-eight hours. Only the center of the slide was exposed to the x-rays, since the ends were protected by metal screens. These ends thus served for controls. In the first experiments, agar slants were prepared from the slides after incubation. They checked the visible observations throughout.

The slight discrepancy in results may be attributed to: (*a*) collection of bacteria in clots and concentration differences; (*b*) differences in x-ray tubes, since two different tubes were used. Both tubes, however, were of the same type.

CONCLUSION

It is apparent that x-rays are lethal to bacteria and that different bacteria show varying degrees of resistance to x-rays. No general conclusion can be made concerning this latter effect, owing to the small number of organisms studied.

The reason why such a long exposure to x-rays is necessary to produce bactericidal action is that much less energy is given off by an x-ray tube than by electric sparks and arcs used in the production of ultra-violet radiation. Most of the radiation emitted by the x-ray tubes used were of 0.63 Å and 0.71 Å wave-length, and their relative intensities were 39 and 63, respectively.

Since the completion of this research, it has come to the attention

[3] Described in Park and Williams, Pathogenic Micro-organisms, 1924 Edition, under "The Hygienic Laboratory Method of the Standardization of Disinfectants."

of the author that a similar investigation was carried out in Germany by Schepmann and Flecke, whose paper appeared in the Klinische Wochenschrift for August 27, 1926. They found that for the same "dosis" x-rays of shorter wave-length were less effective than those of longer wave-length.

These authors employed much more intense (*i.e.*, more penetrating) x-rays than were used in this work, and it is likely that the energy distribution for the different wave-lengths they employed is different than for those used in this work. Consequently, the results of the two researches are not strictly comparable. In spite of this, however, it is significant that the results in both researches agree very satisfactorily for *E. coli*, *Staphylococcus aureus* and *Serratia marcescens* (*B. prodigiosus*). For *B. pyocyaneus* they do not agree in the relative amount of time required to kill the bacteria. In general, however, Schepmann and Flecke arrive at the same conclusions as those determined in these experiments, *i.e.*, that x-rays are lethal for bacteria, and that different bacteria show varying degrees of resistance to x-rays.

The author wishes to express his sincere appreciation for the kind assistance of Dr. M. P. Horwood of the Department of Biology and Public Health and of Dr. W. P. Allis of the Department of Physics of the Massachusetts Institute of Technology. They have assisted with innumerable suggestions concerning the technique employed and with the interpretation of the results obtained.

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ENCEPHALITIS PERIAXIALIS DIFFUSA OF SCHILDER

Report of Two Cases with Anatomical Findings[1]

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Schilder (1) gave the first description of this strange malady in 1912 and distinguished it from the large group of undifferentiated diffuse cerebral scleroses. Not very many additional cases were published in the next ten years, but in 1924 articles by Collier and Greenfield (2) and by Bouman (3) aroused renewed interest in the condition, and since then more than twenty case histories have been published. In the last year additional light has been thrown on the subject by Stewart, Greenfield and Blandy (4), Ferraro (5), Schaltenbrand (6) and Symonds (7).

Schilder's disease is a pathological-anatomical entity, not a clinical entity. It may be defined as a process which causes large areas of myelin destruction in the central white matter of the cerebral hemispheres. These lesions are sharply separated from the cortex by a thin layer of intact white matter, the arcuate fibers. The axis-cylinders are less severely involved and may be preserved after the myelin sheath has been entirely destroyed. In regions where the process is active, lymphocytes and even plasma cells are collected about the small blood vessels, and fat-laden phagocytes are present in great numbers. The disease may start in any part of the brain, although the first descriptions indicated that the occipital lobe was most often the seat of the initial lesion. The two hemispheres are usually affected symmetrically. Small foci may be found in the brain-stem and basal ganglia and the cortex is sometimes affected, but such lesions are always of secondary importance. Fresh lesions are soft, but in cases of long standing the glial scar may be very dense. Secondary degeneration may be absent in acute cases, but is usually present when

[1] Submitted for publication early in the fall of 1928.

the disease has been of long duration. The histological features are very similar to those of disseminated sclerosis and the most obvious distinction lies in the greater size of the lesions and their tendency to be continuous and symmetrically situated. Schaltenbrand has recently given a very careful analysis of the details of the process and of the part which each cell type plays. The reader is referred to his paper.

The clinical characteristics of this condition are subject to great variation. Hereditary factors are usually absent, but Haberfeld and Spieler (8) stated that a sister of their patient was suffering with the same disease, and Ferraro and Symonds have described periaxial encephalitis in siblings. The onset may be delayed until middle age, although children and young adults are most commonly affected. The course is usually subacute, the average duration being a little over a year, but a case is described by Stewart, Greenfield and Blandy in which death occurred eight days after the onset. It is generally believed that the disease is invariably fatal, but remissions are reported by Symonds, and Marie and Foix (9) have described a case in which the symptoms were arrested for ten years. Bouman states that the symptoms are so variable that it is impossible to discover an approximate unity in the diversity, but Collier and Greenfield have attempted to define the clinical picture as follows:

> A malady usually occurring in children and young subjects with no tangible factors or antecedents. The onset is a few days, the course progressive with some remissions to a fatal issue, the duration from a few months to three years. The chief early sign is cerebral blindness which becomes complete, to which is added mental reduction and increasing spastic paralysis. Unsteadiness from parietal involvement and deafness from temporal involvement may be conspicuous. The amentia increases and passes into coma which terminates the illness. The condition, usually bilateral, may commence on one side or be confined to one side.

This description may be drawn somewhat too closely, but it has the virtue of emphasizing the most characteristic features. The symptoms point to the cerebral hemispheres and not to the brainstem, basal ganglia or spinal cord. Hemiplegia, hemianesthesia, hemianopia, aphasia and apraxia are common symptoms, and it is usual for the disturbances to be bilateral. Cortical blindness is very characteristic but not always present. Apathy, stupor, disorienta-

tion, screaming, forced laughter and weeping may occur and, indeed, the mental symptoms are frequently very prominent. Before the end practically all cerebral functions are abolished and the patient shows bilateral spastic paralysis, loss of vision and loss of speech. A remarkable feature is the increased intra-cranial pressure which is found in a considerable number of all cases. Symonds has suggested that the apparent papillo-edema which has been observed in such cases may be due not to intra-cranial pressure, but may merely represent a local change in the optic nerve. This explanation cannot be entertained in regard to the first case described below in which the evidences of increased intra-cranial pressure were overwhelming. Spinal fluid changes are not striking. A few cells are sometimes found and a moderate increase in globulin. More often the fluid is quite normal. The spinal fluid pressure is generally increased.

The etiology is, needless to say, entirely unknown; indeed, no plausible theories have been advanced. It is possible that this condition may have some relation to disseminated sclerosis or to the so-called acute disseminated encephalomyelitis. Familial cases, no doubt, depend upon inherited factors, but it may well be questioned whether they are not of an essentially different nature from the non-familial cases.

The following case histories are published by the courtesy of Dr. Walter E. Dandy on whose neuro-surgical service the patients were studied.

Case history 1. (U. 11887—Path. 9830). *Boy of 14 years developed headache, internal squint, weakness of both legs and of left arm, bulbar palsy, increased tendon reflexes, bilateral extensor response, papillo-edema and finally stupor. Death from respiratory paralysis after six weeks. Autopsy: Periaxial Encephalitis.*

O. W., a school boy, 14 years old, was admitted to the neuro-surgical service of Dr. Dandy May 1, and died May 3, 1927. The complaint was headache and paralysis of the legs. The patient's three siblings and parents were all quite healthy and no disease of the nervous system had been previously noted in the family. The patient suffered a severe attack of chicken-pox late in December, 1926, and was unable to go to school for 3 weeks. His father believes that he was never quite well after this illness, although there were no definite nervous symptoms until the middle of March, 1927, when the patient began to complain of headache and blurred vision associated with violent attacks of vomiting. About April 7, weakness of the left arm and then of both legs was noticed and the patient was soon unable to walk. Difficulty in swallowing and in speech developed

about this time. There was some tendency to retention of urine. Lumbar puncture was performed several times giving transient relief from the headache each time. The spinal-fluid Wassermann test was negative.

On examination the boy was found to be poorly nourished and small for his age. He was somewhat stuporous but screamed when disturbed. Nevertheless, it was possible to secure some degree of coöperation in the examination. Pulse 60, temperature 98°F., respiration 20.

Cranial nerves. I. Sense of smell preserved.

II. Pupils of moderate size, equal and circular, react to light very promptly. Vision sufficient to read half-inch print at 12 inches. Fields of vision seemed to be normal, but coöperation was not satisfactory. Optic nerves greatly swollen, measuring 3 diopters above the retinae. The veins were engorged and tortuous and there were numerous large and small hemorrhages about the discs.

III, IV, VI. No ptosis of the lids. Both eyes rotated inward. Attempt at lateral movement caused merely a few nystagmoid jerks.

V. No loss of motor or sensory function made out.

VII. Marked loss of tone in right side of face and some weakness.

VIII. Normal.

IX, X, XI. Great difficulty in swallowing. Pharyngeal reflex absent. Voice nasal and hoarse. Soft palate did not move on phonation.

XII. Tongue in mid-line. Could not be protruded.

Motor system. The musculature was well developed and showed no atrophy. Passive movements revealed increased muscle tone in both legs and also less definitely in the left arm. The neck was not stiff. Strength was very much diminished in the legs and the left arm was almost entirely paralysed, only a feeble contraction of the flexors of the wrist and elbow being possible. The patient could not sit up or stand, apparently because of general weakness. No ataxia could be demonstrated. No tremor or other involuntary movement was noted. There was severe weakness of the bulbar muscles as noted above. Micturition was delayed.

Sensory system. No satisfactory tests of sensibility could be made because of the stuporous condition of the patient. He appeared to be able to feel the prick of a pin equally well on either side of the body.

Reflexes. Biceps, and triceps reflexes somewhat exaggerated on the left side. The knee and ankle jerks were increased on both sides and an ankle clonus was elicited with ease. The plantar response was typically extensor on both sides. Abdominal reflexes could not be elicited.

The general physical examination of the chest and abdomen revealed nothing of importance. B.P. 100/76, W.B.C. 9200, Hb. 95 per cent.

No change occurred in the patient's condition until May 3 when the respiration suddenly fell to 12 per minute. He was taken to the operating room and a ventricular puncture was made for the relief of pressure. A large amount of fluid was released and respiration improved at once, but 30 minutes later grew slow and ceased.

Gross anatomical findings. Post-mortem examination (Dr. J. H. Bumstead) 6 hours after death. Permission for the removal of the brain alone was secured. The arachnoid was edematous and the cortical veins greatly engorged. Some flattening of the convolutions was evident especially over the right hemisphere which was swollen so that the falx was displaced towards the left. A moderate

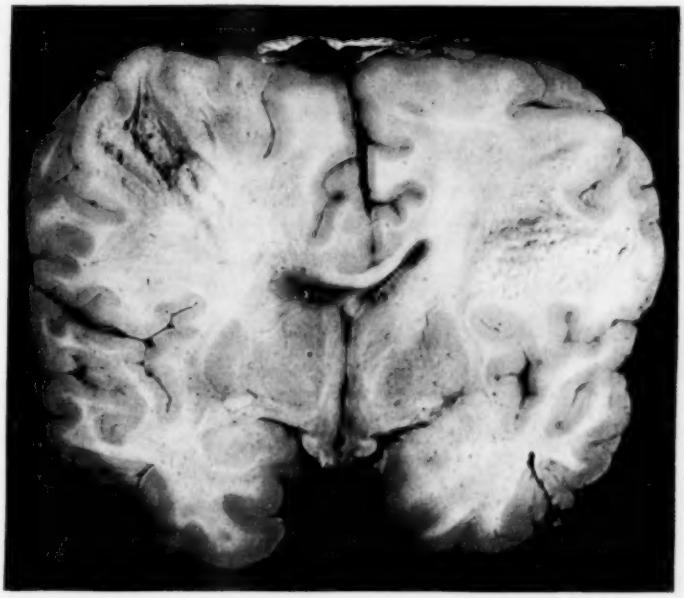

FIG. 1. CASE 1. SECTION 6, SHOWING LARGE ADVANCED LESIONS IN EITHER HEMISPHERE WITH COMPRESSION OF THE LATERAL VENTRICLES

The falx is displaced to the left. The illustration is transposed as regards right and left.

cerebellar pressure cone was present. The vessels at the base were normal and no thrombi could be found in the dural sinuses. The spinal cord and retinae were unfortunately not removed. After fixation the brain was cut into coronal sections 1 cm. in thickness. There were 13 sections in all. Two extensive lesions were found in the right hemisphere. One of these occupied the white matter of the frontal lobe and extended backwards 4 cm. It involved almost all the white matter in the lower half of the lobe and attained a diameter of over 3 cm. The affected tissue was soft on palpation and slightly yellowish. When closely ex-

amined, it was seen to consist of a fibrous, spongy material the interstices of which were filled with a gelatinous liquid which oozed from the cut surface. In places near the center of the lesions the tissue was too soft to cut smoothly and was torn by the knife. These areas were somewhat translucent so that when the section was held up to the light some light was transmitted. The softened areas were sharply separated from the cortex by a thin layer of white matter, the arcuate fibers, which seemed to be well preserved. Where the lesions did not approach

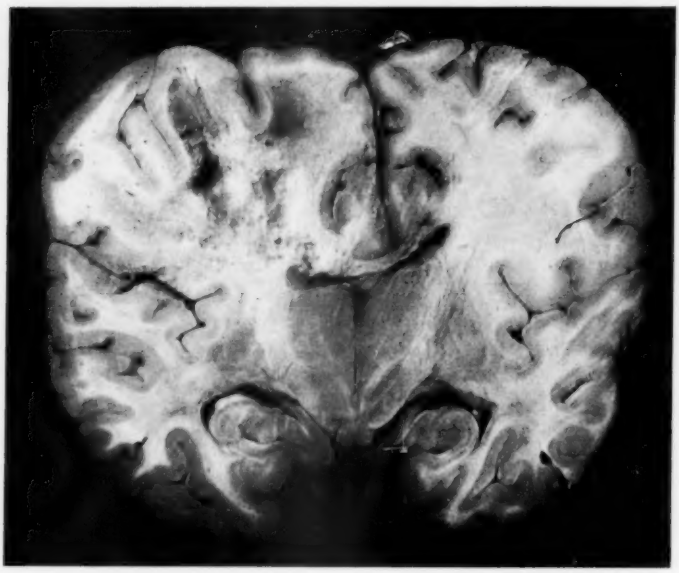

FIG. 2. CASE 1. SECTION 7, SHOWING A LARGE SOFT LESION IN THE RIGHT HEMISPHERE EXTENDING INTO THE CORPUS CALLOSUM

The illustration is again transposed

the cortex, they were not very clearly defined and seemed to fade out gradually. Around the margins of the lesions there was often a slight brownish discoloration which seemed to represent the earliest stage in the process. Another massive lesion of the same kind was found beginning 1 cm. behind the first one (Figs. 1 and 2). This extended all the way to the occipital pole and reached a diameter of 6 cm. It involved most of the white matter of the frontal and parietal lobes and then becoming smaller in the occipital region was confined to the cuneus. In the left hemisphere a similar lesion began in the frontal lobe and extended back-

FIG. 3. CASE 1. MALLORY'S GLIAL FIBER STAIN. LOW-POWER MICROPHOTOGRAPH SHOWING THE GLIAL RETICULUM

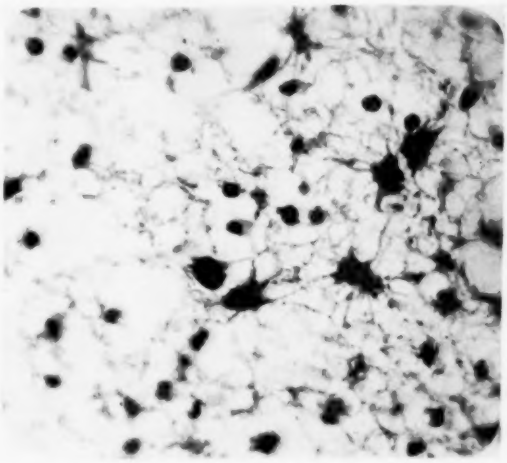

FIG. 4. CASE 1. HEMATOXYLIN AND EOSIN. HIGH-POWER MICROPHOTOGRAPH SHOWING THE HYPERTROPHIED ASTROCYTES WITH MULTIPLE NUCLEI

wards 3 cm. This lesion reached a diameter of 3 cm. A very small lesion was found in the left gyrus fusiformis. All of these 4 lesions had exactly the same gross appearance.

Histological findings. Numerous blocks were cut from all parts of the brain and paraffin, celloidin, and frozen sections made. The following stains were employed; hematoxylin and eosin, Nissl's toluidin blue, Kulschitski's modification of Weigert's myelin stain, Loyez' myelin stain, Herxheimer's fat stain, Mallory's glial fiber stain, Bielschowski's axis-cylinder method and the mucicarmine of Meyer.

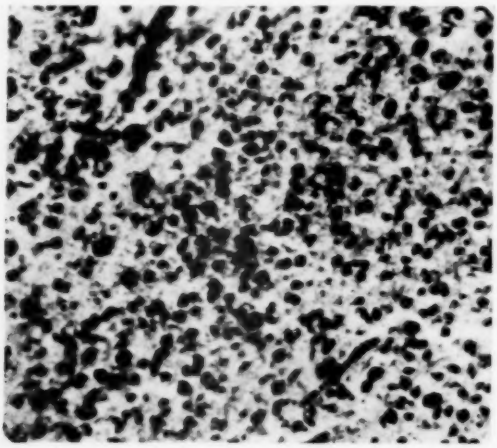

FIG. 5. CASE 1. HERXHEIMER FAT STAIN. LOW-POWER FIELD OF SEVERELY DEGENERATED AREA, SHOWING GREAT NUMBERS OF PHAGOCYTES LADEN WITH LIPOID PRODUCTS

The details of the process were everywhere the same. In well advanced lesions there was complete disappearance of the myelin. The tissue was composed of a coarse reticulum formed by the fibrous processes of giant astrocytes (Fig. 3). These cells were present in increased numbers and very much swollen. Many of them contained more than one nucleus (Fig. 4). Small fat granules were seen in their cytoplasm. In the interstices of this reticulum a vast number of phagocytes were collected (Fig. 5). These were distended with large lipoid droplets and their oblong nuclei were displaced to the periphery of the cell body. It is now generally held that these *Gitter* cells arise by a transformation of the microglia. Rod cells were also seen with numerous fatty globules in their cytoplasm. Both large and small lipoid globules were seen lying loosely scattered throughout the tissues.

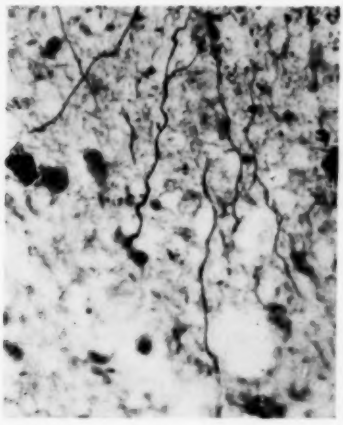

FIG. 6. CASE 1. BIELSCHOWSKI'S AXIS-CYLINDER STAIN. PARTIAL PRESERVATION OF AXIS-CYLINDERS IN COMPLETELY DEMYELINATED AREA

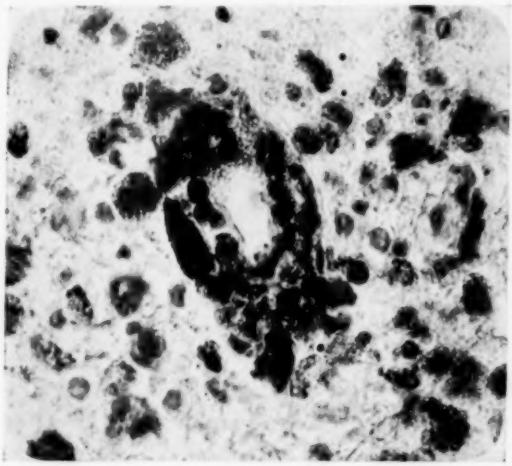

FIG. 7. CASE 1. HERXHEIMER FAT STAIN. COLLECTION OF FAT-LADEN PHAGOCYTES IN ADVENTITIA OF SMALL BLOOD VESSEL

NIV. OF ICH.

Many naked axis-cylinders could be demonstrated in completely demyelinated areas, but most of them were twisted and swollen and some were fragmented (Fig. 6). They were, of course, greatly reduced in number. In the center of the most advanced lesions the glial net-work was disintegrated. In such regions numerous swollen, round cells without processes were seen which often contained fatty granules. These seemed to be degenerating astrocytes.

In the marginal zones of the lesions where the tissues were merely slightly discolored without softening, the myelin sheaths were only partially destroyed. The astrocytes showed little swelling and only one nucleus. The phagocytes

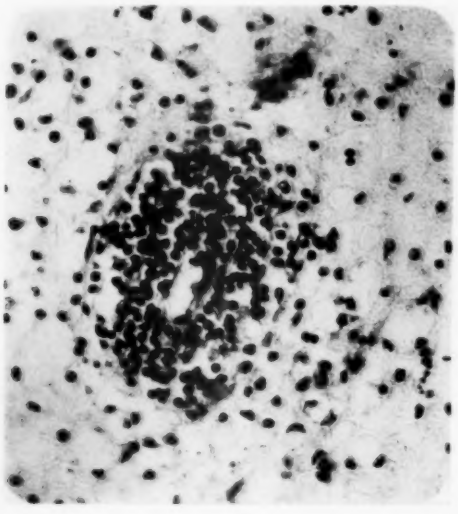

FIG. 8. CASE 1. HEMATOXYLIN AND EOSIN. CLUSTER OF LYMPHOCYTES ABOUT A SMALL VESSEL

were collected about the small blood vessels, but were not scattered throughout the tissues as in the center of the lesions (Fig. 7). Clusters of lymphocytes were found in the adventitial spaces either among the fat-laden phagocytes or alone. No leucocytes or plasma cells were discovered (Fig. 8). In between bundles of nerve fibers which were only mildly involved numerous cells with large round nuclei were found lying in rows. Each was surrounded by a clear zone which did not stain. These are the so-called oligodendroglia which, as Penfield has shown, undergo acute swelling in numerous pathological conditions of the nervous system. Schaltenbrand recently claimed that this is a mucinoid degeneration. We were unable to demonstrate the mucin reaction in these cells.

Where the lesions approached the cortex there were sometimes mild changes in the deeper cortical layers. The pyramidal cells were shrunken and stained diffusely. A few fat-laden phagocytes were seen about the vessels, but these changes were never severe. The arcuate fibers were sometimes partially demyelinated where they were in contact with an extensive lesion, but the rule that they are preserved usually obtained (Fig. 9). The anterior commissure was completely demyelinated. The brain-stem, cerebellum, internal capsule, peduncles, pyramids, optic radiations, optic tracts, optic nerves, thalamus, caudate and lenticular nuclei were all intact. The corpus callosum was involved by the lesion in the right hemisphere, but the lesion did not extend across to the left side.

FIG. 9. CASE 1. LOYEZ' MYELIN SHEATH STAIN. SHOWING CHARACTERISTIC LIMITATION OF LESION BY ARCUATE FIBERS

SUMMARY OF THE ANATOMICAL FINDINGS

The right hemisphere contained 2 massive lesions occupying the white matter of the frontal, parietal and occipital lobes, and the left hemisphere revealed one large one in the frontal lobe and a very small one under the gyrus fusiformis. These were soft and spongy and oozed with a gelatinous liquid. The most advanced lesions—and therefore the oldest—were those in the superior frontal lobes.

Histologically, there was complete destruction of the myelin sheaths in the center of the lesions. Some of the axis-cylinders were, however, preserved and there was no secondary degeneration. The affected tissue was composed of a very coarse glial fiber reticulum in the inter-

stices of which an enormous number of phagocytes loaded with lipoid products were collected. The astrocytes were hypertrophied and frequently contained several nuclei. In the center of very severe lesions they had lost their processes and were undergoing degeneration. The inter-fascicular glial cells were swollen. Many of the blood vessels contained extensive collections of phagocytes in their adventitial spaces, and perivascular lymphocytic infiltrations were also very numerous.

Case history 2. (U. 19806—Path. 10500.) *Boy of 2 years developed internal squint. Later sudden weakness of left leg following a fall. Incomplete recovery in 6 weeks. At age of 2 years and 10 months sudden paralysis of right arm and leg. Gradual improvement for 5 weeks. Then increasing weakness irritability and finally stupor. On examination at age of 3 years paralysis of both legs, slight weakness of the arms, speech defect, left 6th nerve palsy, increased tendon reflexes, ankle clonus, bilateral extensor response, and stupor. Operation. Death. Periaxial Encephalitis found at autopsy.*

D. B., aged 3 years, was the second child of healthy parents. One sibling, aged 4½ years, was quite well. The patient had never been ill before the present illness and his birth and early development had been normal in every respect. In March, 1927, the mother had noticed that the child's left eye turned inward, but no other symptoms were observed at that time. July 18, 1927, the child fell backwards off of a curb-stone striking the back of his head and remaining unconscious for one hour. He was put to bed and the next day was found to be almost completely paralyzed in the left leg. There was no bleeding from the nose or mouth and the child's head was not cut or bruised. The mother did not notice any convulsive movements. The weakness improved gradually and after 6 weeks the child seemed to have made a complete recovery except for a slight limp in the left leg. His mother thinks that his condition remained stationary for about 6 months. Then she noticed that he showed a tendency to walk on the balls of his feet and a growing clumsiness in the use of his legs. In May, 1928, when the child was walking across the floor holding his mother's hand, he suddenly released his grasp and fell, striking the left side of his head. He was not unconscious and did not have any convulsive movements, but when picked up the right arm and right leg were found to be completely paralysed. Improvement soon began and within 4 days he had recovered some power of movement, but was never able to walk after this last episode. About the middle of July, he seemed to grow weaker so that he could not hold up his head and could not sit up well. His speech became difficult to understand and he grew very irritable and somewhat stuporous. He made no complaint of headache and vomited only once, on July 24. He was admitted to the neuro-surgical service of Dr. Dandy on July 31, 1928.

On examination the patient was found to be a boy of 3 years, poorly nourished

and poorly developed. Temperature 99°, pulse 120, respiration 28. He was entirely uncoöperative, screaming and resisting the examiner.

Cranial nerves. II. Pupils moderate in size, equal and circular. They reacted to light with a good excursion. Vision could not be tested, but it was certainly not lost, for the child would follow objects with his eyes. The fields of vision

FIG. 10. CASE 2. SYMMETRICAL LESIONS IN THE PARIETAL LOBES

could not be tested. Optic nerve heads were of good color and showed no elevation, but there was some blurring of the margins.

III, IV, VI. The left eye could not be abducted beyond the mid-line. No other oculomotor weakness.

V, VII. Normal?

VIII. Hearing seemed good. Not tested quantitatively.

IX, X, XI, XII, Normal?

Motor system. The musculature was poorly developed and rather soft, espe-

cially in the legs where there was apparently some slight atrophy. On passive movement muscle tone seemed to be below rather than above normal. The feet were held in the equinus position, the great toes being dorsiflexed. The legs were almost completely paralysed and could not be lifted from the bed. The arms were moved freely, but seemed to be clumsy; whether this was due to weakness or to ataxia was very difficult to decide. The fingers could not be used for any skilled act. The left hand was used in preference although the child was naturally right-handed. The trunk muscles were too weak to permit the child to sit up and the head tended to fall forward on the chest. Speech was dysarthric, but could be understood. There was urinary incontinence

Sensory system. A pin prick could be appreciated on either side of the body, but no other sensory tests were possible.

Reflexes. Biceps, triceps, knee and ankle jerks were all exaggerated on either side and about equal. There was bilateral ankle clonus and bilateral extensor response on plantar stimulation.

Physical examination of the chest and abdomen revealed no signs of disease. Urine negative. W.B.C. 9700, PMN. 63 per cent, Hb. 70 per cent, R.B.C. 3,500.000. Blood Wassermann negative. Spinal fluid, cells 5–7; globulin 0. Pressure not increased. Wassermann test negative. Roentgenogram of the skull negative.

The bilaterality of the signs suggested involvement of the brain-stem and on August 1st the posterior fossa was explored. Nothing to account for the patient's symptoms was found. The child failed to rally and died on the next day.

Gross anatomical findings. The autopsy was performed by Dr. S. S. Blackman. No evidence of disease outside the nervous system was discovered. Externally the brain showed no abnormality. The convolutions were full and rounded. The meninges were delicate and grossly the arteries at the base were normal. There was no outspoken flattening of the convolutions and no cerebellar herniation. On section the typical picture of Schilder's disease was at once revealed. Most of the white matter of the frontal and parietal lobes was soft and spongy with the exception of the narrow band of arcuate fibers underlying the cortical convolutions. These seemed to have been spared throughout. The most advanced lesions were found in the superior parietal lobes where the tissue was reduced to a reticulum of extraordinary delicacy suggesting a spider web (Fig. 10). In the temporal lobes the process was just beginning and the white matter was only slightly softened, but in the occipital lobes advanced lesions were seen which involved both the external and internal sagittal marrow. A small hemorrhage was found in this region on the right. The process was continuous, although more advanced in some regions than in others, and both hemispheres were symmetrically affected. The cortex was not involved. The corpus callosum, the external capsule and tapetum were all softened, although the capsula interna was intact. No gross changes were seen in the basal ganglia, brain-stem or cerebellum.

Histological findings. The histological picture was almost identical with that found in case 1 with several minor exceptions due to the longer duration of the process. The glial reticulum was in general much denser and the glial nuclei were more numerous. These glial cells possessed small round nuclei and their cytoplasm which was very scanty did not contain any fat granules. The giant astrocytes with multiple nuclei, which were so prominent in case 1, were not seen, nor were any of the large globoid cells without processes which we considered to be degenerating astrocytes. Myelin, was, of course, entirely lacking in most of the affected areas, but here and there small areas could be seen in the Weigert-stained preparations where a small number of myelin sheaths were preserved. The fat stains revealed only an occasional clump of fat-laden phagocytes which were usually collected in the adventitial spaces of the small blood vessels. This was in marked contrast to the findings in case 1, in which the whole microscopic field was crowded with innumerable phagocytes loaded with lipoid products. No perivascular lymphocytic infiltrations were found.

SUMMARY

A brief description is given of the clinical and anatomical characteristics of Schilder's periaxial encephalitis and two case histories are reported. The first case ran a very acute course of six weeks and was terminated by death from increased intracranial pressure. The anatomical changes were somewhat atypical in that the process was not continuous, and four discrete lesions were found. In this respect the case was almost identical with that reported by Schaltenbrand.

Our second case was quite typical in respect to the morbid anatomy, but the clinical picture was unique and serves to illustrate the extraordinary variability which this disease may exhibit. The child had two sudden falls followed by paralysis and in one case by loss of consciousness. On the first occasion the paralysis was not noted until the next morning, but the second time it was discovered at once. Each time marked improvement followed very promptly, and once this amounted to substantial, if transient, recovery. Such an apopleptic onset has not been described in Schilder's disease previously. The anatomical picture was quite typical in this case.

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DEXTROSE TOLERANCE TEST IN EXPERIMENTAL TOXEMIA[1]

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The ill effects of infection upon the carbohydrate metabolism of patients suffering from diabetes mellitus have been known for many years. Although insulin has altered the clinical management of cases, the rôle of infection in disrupting the diabetic metabolism still remains obscure. It has seemed natural to assume that during infection the processes occurring in the diabetic might be duplicated to a lesser extent in the non-diabetic. In the absence of any adequate criteria for measuring the carbohydrate metabolism, the curve of blood-sugar levels following ingestion or injection of dextrose is usually taken as a means of comparison. These dextrose tolerance curves of diabetics and of normal humans and animals are known.

Utilizing the blood-sugar curve following intravenous dextrose injection Tisdall, Drake and Brown (1) (2) have found a distinct lowering of the dextrose tolerance in non-diabetic infants suffering from diarrhea and intestinal toxemia. Menten and Manning (3) and Zeckwer and Goodell (4) have found an increased blood sugar following intravenous injection of dead bacteria.

Tisdall, Drake and Brown (5) have also found in dogs that the subcutaneous injections of diphtheria toxin or of histamine will decrease the carbohydrate tolerance. Similar effects were obtained by them through dehydration and through the production of severe purgation with magnesium sulphate, jalap or castor oil. Simple fever, however, as produced in the first hours after subcutaneous diphtheria toxin and before toxic symptoms appear, they found to increase the carbohydrate tolerance.

Pemberton and Foster (22) have shown the removal of foci of infection in several cases of arthritis to be accompanied by a return of a previously lowered dextrose tolerance to normal.

[1] Received for publication February 11, 1929.

More recently, Sweeney and Lackey (6) have shown that rabbits receiving enough subcutaneous diphtheria toxin to produce death in 5 to 7 days show a steadily decreasing tolerance for dextrose administered by stomach tube, the blood-sugar levels after administration rising on succeeding days. In a later experiment, Sweeney (7) showed that normal dextrose tolerance curves could be obtained from similarly intoxicated animals if insulin were given in the ratio 1 unit for each 2.5 gm. of dextrose.

EXPERIMENTAL

Since the common infections of the diabetic patient are usually of the Gram-positive coccus group, the following experiments were made of the dextrose tolerance of rabbits following the intravenous injection of streptococcus toxic filtrate produced by growing the streptococcus erysipelatis (strain B-13)[2] in tryptic ferment beef broth for 24 hours, filtering through a Berkefeld filter and then heating at 55°C. for thirty minutes to ensure sterility. Of the filtrate 10 cc. were injected into the marginal ear-veins of the rabbits in these experiments. Larger doses produced severe diarrhea and death which was not desired, since the previous workers have rather well established the effect of lethal toxemias on the dextrose tolerance. Because the large amounts of broth might have an effect, the controls were made upon rabbits injected with a similar amount of plain tryptic ferment beef broth in which no organisms had been grown. As a further control, four animals were injected with a mixture of toxic filtrate and an excess of erysipelas antiserum.

The rabbits were kept on standard diets of oats, hay and cabbage before the experiments, since it has been shown that the dextrose tolerance is lowered by a diet low in carbohydrates (8) (9) (10) (11). Water was constantly available in all the cages to eliminate a factor of dehydration which has been reported as altering the dextrose tolerance (5) (11). At the time of the intravenous injection of the toxic filtrate or the control broth, the cages were carefully cleaned of all food and the animals starved during the tests. Ten grams of dextrose

[2] I am deeply indebted to Professor Harold L. Amoss for furnishing me with this strain and for his guidance in these experiments.

in 50 cc. of water were directly introduced into the stomachs of the animals through a No. 18 French catheter. One-tenth cubic centi-

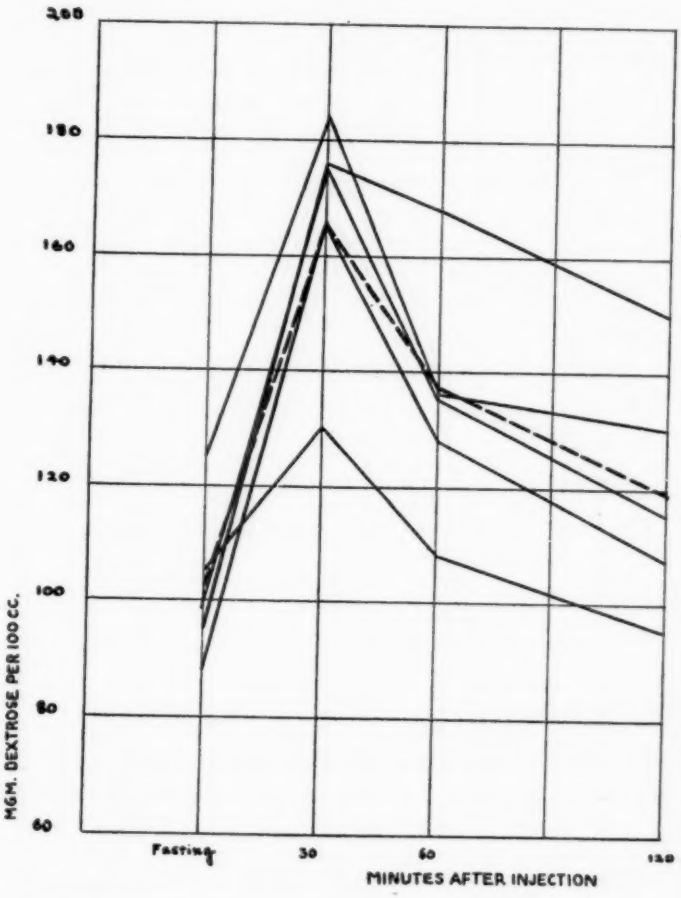

FIG. 1. DEXTROSE TOLERANCE OF NORMAL RABBITS—24 HOURS FASTING

meter of blood was obtained from the marginal ear-vein just prior to the administration of the dextrose and at 30, 60 and 120 minutes after.

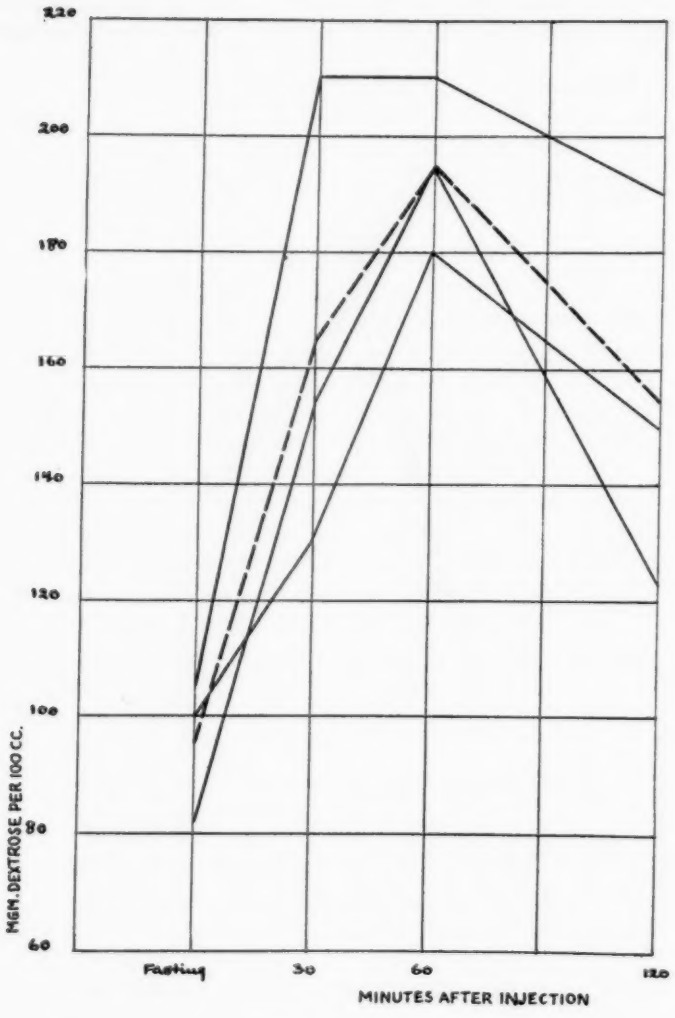

FIG. 2. DEXTROSE TOLERANCE OF NORMAL RABBITS—48 HOURS FASTING

Sugar determinations were made by the micro-modification of the Folin-Wu method (12) (13).[3]

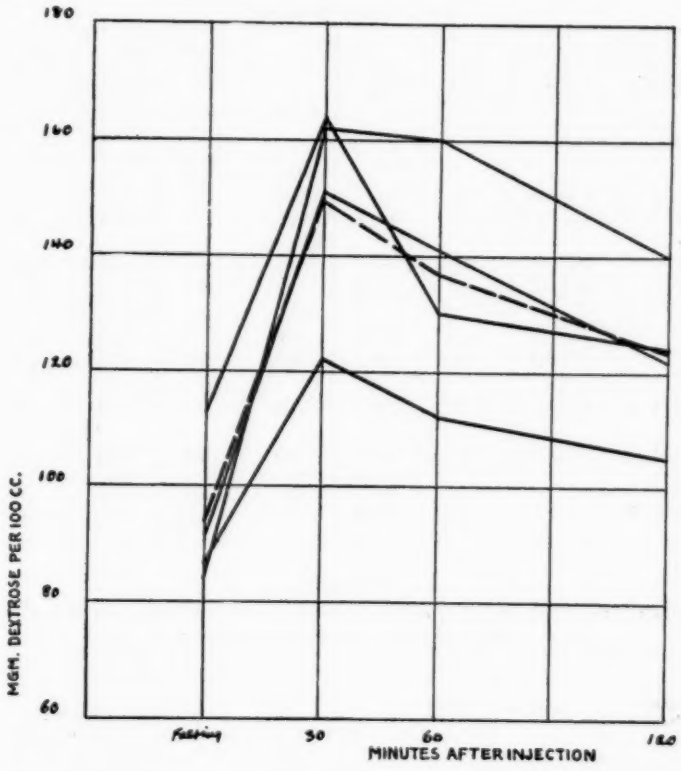

FIG. 3. DEXTROSE TOLERANCE OF RABBITS—24 HOURS FASTING AFTER INJECTION OF TOXIN-ANTITOXIN MIXTURE

Table I (figs. 1 and 2) shows the results of the first series of controls and Table II (fig. 3) summarizes the results of the second set. The results are in conformity with the normal curves generally obtained from animals and humans.

[3] I wish to thank Dr. W. A. Perlsweig for the use of his laboratory.

TABLE I

Dextrose tolerance test on fasting rabbits 24 and 48 hours after the intravenous injection of 10 cc. tryptic ferment broth

RABBIT NUMBER	DATE	HOURS AFTER INJECTION	RECTAL TEMPERATURE	BLOOD SUGAR			
				Fasting	After 10 grams dextrose		
					30 minutes	60 minutes	120 minutes
			°F.	*mgm. per 100 cc.*	*mgm. per 100 cc.*	*mgm. per 100 cc.*	*mgm. per 100 cc.*
1	May 21	24	102	100	175	135	115
	May 22	48	102.5	100	130	180	150
2	May 21	24	103	88	165	128	107
	May 22	48	102.8	82	155	195	123
3	May 23	24	102.6	126	184	135	130
	May 24	48	102.2	105	210	210	190
4	May 23	24	102	96	175	168	150
11	May 25	24	101.8	105	130	108	95
Averages		24	102.2	103	166	137	119
		48	102.5	96	165	195	154

TABLE II

Dextrose tolerance test on fasting rabbits 24 hours after the intravenous injection of toxic filtrate plus excess of erysipelas antiserum

RABBIT NUMBER	DATE	RECTAL TEMPERATURE	BLOOD SUGAR			
			Fasting	After 10 grams dextrose		
				30 minutes	60 minutes	120 minutes
		°F.	*mgm. per 100 cc.*	*mgm. per 100 cc.*	*mgm. per 100 cc.*	*mgm. per 100 cc.*
12	June 14	102.8	113	164	130	124
13	June 16	103.2	87	122	112	105
14	June 16	103.2	92	151	141	122
15	June 16	102.6	85	162	160	140
Averages		102.9	94	149	137	123

TABLE III

Dextrose tolerance test on fasting rabbits following the intravenous injection of 10 cc. Streptococcus toxic filtrate

RABBIT NUMBER	DATE	HOURS AFTER INJECTION	RECTAL TEMPERATURE	BLOOD SUGAR			
				Fasting	After 10 grams dextrose		
					30 minutes	60 minutes	120 minutes
			°F.	mgm. per 100 cc.	mgm. per 100 cc.	mgm. per 100 cc.	mgm. per 100 cc.
1	May 15	24	103.2	95	165	195	200
	May 16	48	103.2	115	170	188	173
	May 17	72	102.5	103	151	176	110
2	May 15	24	103.4	60	117	122	115
	May 16	48	104.2	75	135	155	128
	May 17	72	103	80	150	170	83
3	May 29	24	102.5	102	175	210	233
	May 30	48	102.3	119	196	205	220
	May 31	72	101.6	98	145	180	165
5	June 5	24	102.8	63	112	122	114
	June 6	48	102.4	111	200	188	184
	June 7	72	102.2	102	136	184	152
8	June 8	24	102.6	90	120	151	150
	June 9	48	103.2	89	164	162	138
	June 10	72	103	80	124	150	112
9	June 8	24	103	82	122	134	132
	June 9	48	103	81	138	160	118
	June 10	72	103.4	70	164	192	210
10	June 8	24	101.6	85	120	129	144
	June 9	48	102	96	150	142	124
	June 10	72	101.4	95	150	133	120
Averages.....		24	103.2	85	136	156	162
		48	103.6	96	158	168	150
		72	102.8	87	147	166	133

From the data, the lowered dextrose tolerance on the second day of fasting is evident, a point previously brought out by numerous workers (11) (14) (15) (16) (17) (18) (19).

Table III (figs. 4, 5 and 6) shows the results of the dextrose tolerance

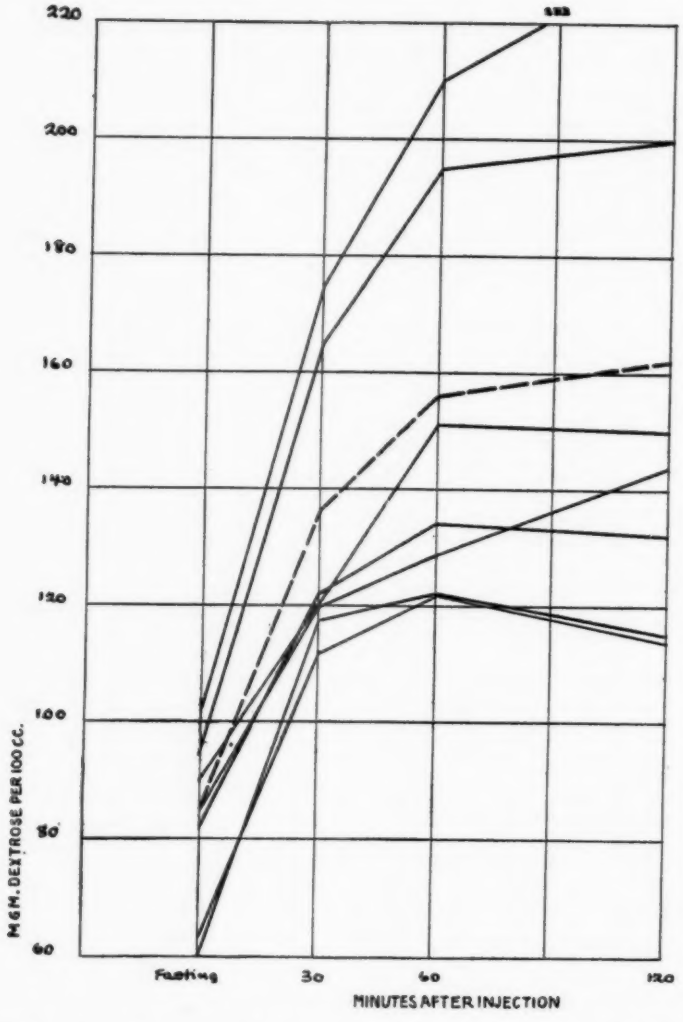

FIG. 4. DEXTROSE TOLERANCE OF RABBITS—24 HOURS FASTING AFTER INJECTION OF STREPTOCOCCUS TOXIN

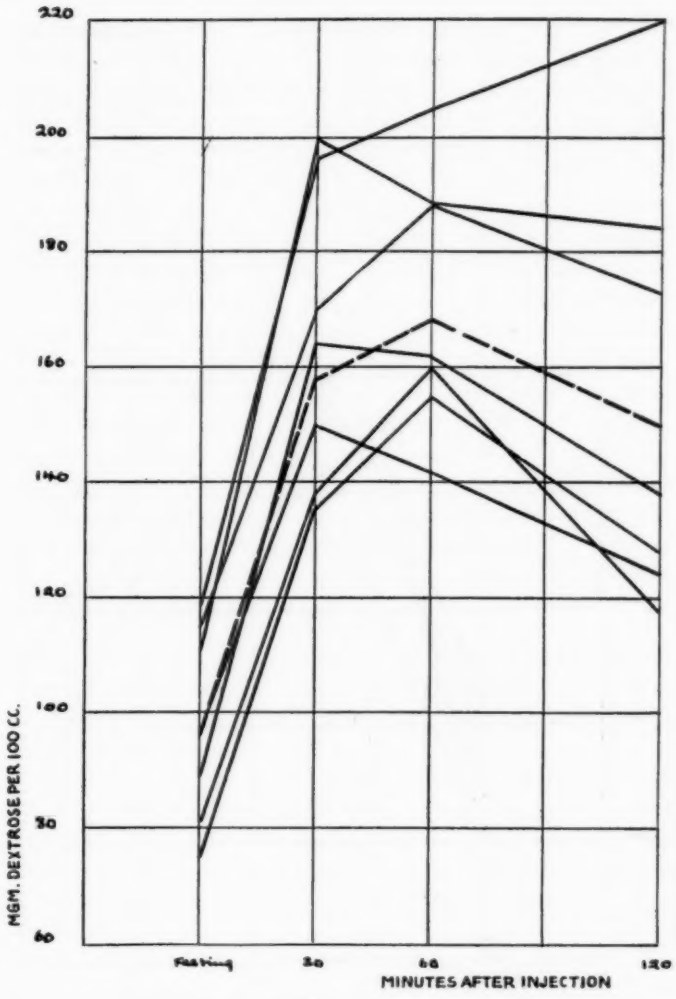

FIG. 5. DEXTROSE TOLERANCE OF RABBITS—48 HOURS FASTING AFTER INJECTION OF STREPTOCOCCUS TOXIN

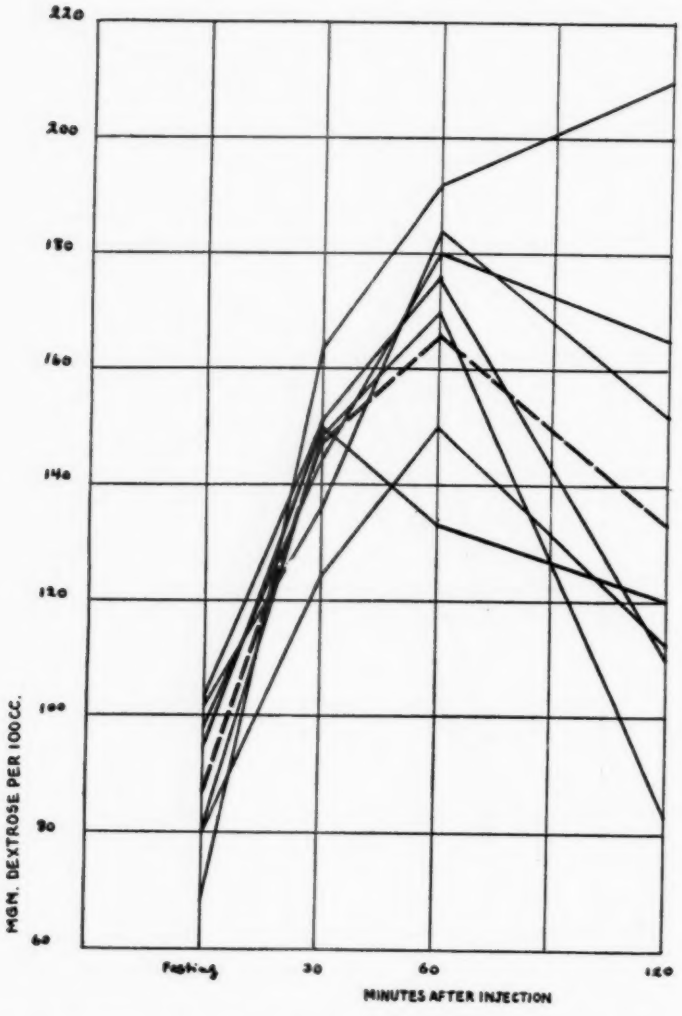

FIG. 6. DEXTROSE TOLERANCE OF RABBITS—72 HOURS FASTING AFTER INJECTION OF STREPTOCOCCUS TOXIN

test on the three successive days after injection of streptococcus toxic filtrate.

On the first day, the blood sugars rose steadily for the first 60 minutes and then remained at an elevated level during the next hour, giving the kind of curve which is commonly considered typically diabetic. At this time, the animals appeared less active than usual and had slight fever (*ca.* 1°F.)

On the second day after injection, there was a less marked rise of the blood sugar during the second half hour after the administration of the dextrose and a distinct drop during the second hour. The animals still showed a slight elevation of temperature but otherwise appeared normal. The blood sugar curves obtained resembled the "pre-diabetic" type of human curve and are here presumably the result of a combination of two factors: the forty-eight hours of starvation and the residual toxemia of the injection.

At the end of three days, the results were similar to those obtained through simple starvation, with a rise during the second half hour but a pronounced fall during the second hour. The animals did not appear in any way abnormal at this time except for the extreme voracity exhibited when they were fed at the conclusion of the experiment.

DISCUSSION

The results of these experiments seem to indicate that the ability of the normal animal organism to remove dextrose from the blood stream may be impaired by an artificially produced toxemia. Since only 20 per cent of the ingested dextrose is utilized in the first 2 to 3 hours (20) (21) and the major portion stored presumably as glycogen, it is likely that in these animals the process of glycogenesis was interfered with by the toxemia, although changes in the peripheral circulation such as those indicated by the studies of Pemberton and his co-workers (23) (24) (25) in patients with arthritis must be considered.

Thus streptococcus toxic filtrate alone, when injected intravenously, lowers the tolerance of rabbits to ingested dextrose, but a mixture of toxic filtrate plus erysipelas antiserum produces no effect. The neutralizing action of the erysipelas serum on this phase of the toxemia is definite.

CONCLUSIONS

1. The dextrose tolerance of rabbits is markedly reduced by toxemia produced by the intravenous injection of streptococcus filtrate.

2. Erysipelas antiserum completely neutralizes the tolerance-reducing effect of streptococcus toxic filtrate.

3. The dextrose tolerance is reduced by fasting.

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BOOK REVIEWS

Gynecology. By WILLIAM P. GRAVES, A.B., M.D., F.A.C.S. Fourth Edition. 1016 pp. $10.50. (*W. B. Saunders Company, 1928.*)

This standard textbook appears again completely revised and beautifully printed. The author has been most thorough and scholarly in his incorporation of the more recent advances and trends of thought in the gynecological field. There are numerous changes. The physiology of the female reproductive organs and their relation to the organs of internal secretion; carcinoma of the uterus; sterility; diathermy; the sedimentation test; and endometriosis are subjects which seem to have been particularly well treated from the newer points of view.

The illustrations are good. There are many new photomicrographs which enhance the value of the sections dealing with normal and pathological changes in the tissues.

The work as a whole gives one the impression that all that is new and sound has been incorporated, together with that which has stood the test of time, into a most logical comprehensive, and attractive treatise. Of course, such a book always leaves one with the wish that, here and there, the author could have devoted more space to present matters in greater detail. But this is a textbook primarily, and as such fulfills its design admirably.

H. F. T.

Diseases of the Skin. A Manual for Students and Practitioners. By ROBERT W. MACKENNA, M.A., M.D., B.Ch. (Edin.) Second edition, revised and enlarged. 452 pp. $7.50. (*The Williams & Wilkins Company, Baltimore, 1927.*)

In judging this book, one must keep constantly in mind the main aim of the author, which primarily is to meet the requirements of the student and the needs of the general practitioner. Recognizing the fact that the student's curriculum is already overloaded, he has attempted to present the various diseases in a concise but often too brief a description. In a book of this kind it may be wise to concentrate on differential diagnoses and dogmatic principles of treatment, but for the sake of the student would it not be still better to emphasize etiology, where it is known, and indicate methods of search for etiological factors where such causes are still unknown. There is very little that is new, either in substance or in arrangement. The illustrations are practically all of a superior order. The book will be found very useful for those for whom it is intended—the student and the general practitioner.

H. M. R.

Syphilis. By HARRY H. HAZEN. Second Edition. 643 pp. $10.00. (*C. V. Mosby Company, 1928.*)

The author's purpose was to write "a small book that covers the whole field of syphilis in an authoritative way." In spite of the comparative small size of the volume, the task was so great that several chapters have been written by different authors who have had wide training and experience in their special fields. Chapters are devoted to lesions of the nails and hair, to the endocrine glands and to the eye. There is also an interesting chapter on syphilis of the genito-urinary organs by Fowler, illustrated with colored plates showing syphilitic lesions of the bladder.

The subject matter is condensed. Elaboration and lengthy discussion are omitted. Over 1700 references are cited, making the book doubly valuable as an aid for further study. There are 595 illustrations, many of which are interesting and instructive. The book is neither cumbersome, nor does it exploit the author's own view; but represents an excellent and exhaustive digest of the medical literature. It is, therefore, well suited as a textbook for students entering on the study of syphilitic infection.

H. W.

Food Infections and Food Intoxications. By SAMUEL REED DAMON, A.M., Ph.D., Associate Professor of Bacteriology, School of Hygiene and Public Health, The Johns Hopkins University. 264 pp. $4.00. (*The Williams & Wilkins Company, Baltimore, Maryland, 1928.*)

In the past twenty-five years the subject of food infections and intoxications has been quite thoroughly investigated and many of our ideas have been completely revised. This new volume clearly presents these modern conceptions. The material is presented under three heads, Part I comprising a description of infections from food, Part II intoxications from food, and Part III zoö-parasitic infections acquired through food, an arrangement that offers the reader the simplest method of studying the subject.

The chapter on botulism is perhaps one of the most interesting. The prodigious amount of research and discussions dealing with these problems has undoubtedly necessitated the reviewing of a vast amount of literature. The author's treatment of this subject is illustrative of the book in general.

The discussions are, in general, clear and concise, and each subject is so presented as to include the phases of etiology, symptomatology, diagnosis, treatment and prophylaxis. The material contained in the book is purposely limited to those diseases in which food acts as essentially the only vehicle through which the etiological agent is spread, without taking into consideration those diseases in which food acts merely as a transmitting agent.

There are necessarily some omissions. There are also a few statements with which all readers might not agree, but the material has been carefully studied and the volume gives our modern conceptions with great clarity.

The book as a whole is quite complete and the literature is up to date. To

those interested in the subject of food infections and food intoxications it should be of very definite value.

W. A. F.

Experimental Pharmacology as a Basis for Therapeutics. A Textbook for Students and Physicians. By Dr. HANS H. MEYER and Dr. R. GOTTLIEB. Second Edition in English, translated by VELYIEN E. HENDERSON, from the seventh revised German edition. 656 pp. $7.00. (*J. B. Lippincott Co., Philadelphia, 1926.*)

Professor Henderson has rendered English-speaking pharmacologists and scientists in general a great service by making available to them so excellent a work as Meyer and Gottlieb's Textbook of Pharmacology. The translator emphasizes in his preface the unique arrangement and remarkable physiological insight of the work. To those of us who are fortunate enough to have read the work in the original the treatment of pharmacology founded upon the physiology and pharmacology of each organ has been very useful. It has been the custom in some laboratories in this country to mould the courses, especially the experimental laboratory work, along the lines of Meyer and Gottlieb. These authors have taken as their keynote the study of drugs according to their effect on the functions of the organs of the body and on the causes of disease, and in this way have hoped to make pharmacology more serviceable to the physician in the treatment of his patient. It is admitted that this method of studying pharmacology leaves out of consideration a large body of facts known to the science and of importance, but not at present applicable, in practical therapeutics. The work is richly illustrated with diagrams of a physiological and anatomic character, a feature which makes the text very valuable for students as well as for teachers.

The translator has followed the German text closely, and it is only in passages where it is very difficult, if not impossible, to translate accurately without some awkwardness, that the English does not run smoothly. Some very useful and appropriate changes have been made in the translation, such as the use of the scientific names and the doses for drugs as given in the tenth edition of the United States Pharmacopeia (1926) and the British Pharmacopeia (1914), instead of the terms and doses used in Germany. The grouping of the references at the end of each chapter is also an added advantage of this translation.

The popularity of this work in German is attested to by the fact that there have been seven editions in fifteen years. It is without doubt the most widely used pharmacological text in Europe, and it will surely find extensive use by both students and teachers in the English-speaking countries.

E. M. K. G.

Diabetic Manual for Patients. By HENRY J. JOHN. 202 pp. $2.00. (*The C. V. Mosby Company, St. Louis, 1928.*)

This small volume of 200 pages contains an excellent condensed discussion of

the salient facts concerning causation and treatment of Diabetes Mellitus. It is intended for use by patients, but should be of even greater value to medical students and to many doctors. There is a valuable chapter entitled "Is There Any Cure?" which should bring many patients to a more reconciled view of their disease.

Insulin is treated in great detail, with many charts and curves of blood-sugar and insulin effect, some of which should be of greater value to students than to patients. The statement that a single insulin reaction should be regarded as an "accidental occurrence," which necessitates no change in diet or dosage, seems to be too general. Mild reactions probably may be allowed to pass without any change, but a severe reaction surely demands that steps should be taken to avoid recurrence.

The author has used liberally the graphic method of illustration. Especially effective should be the graphic presentation of the composition of some of the common food stuffs.

The book is a welcome addition to the group of Diabetic Manuals, both in form and content.

E. J. L.

Osler's Modern Medicine. Third Edition. Re-edited by Thomas McCrae, M.D. Assisted by Eleanor Funk, M.D. *Volume VI. Diseases of the Nervous System, Diseases and Abnormalities of the Mind.* $9.00. (*Lea & Febiger, Philadelphia, 1928.*)

This volume contains some excellent clinical articles written by leading neurologists of the English-speaking world. A broad introduction with emphasis on the physiology of the nervous system is written by Dr. Lewellys F. Barker. Important chapters are contributed by Spiller, Joseph Collins, Cushing, Gordon Holmes, Edward Taylor, Buzzard, Symonds and Jelliffe. The splendid monograph of the late Henry M. Thomas on Diseases of the Cerebral Bloodvessels is retained. A new article on epidemic encephalitis has been added by Ramsay Hunt, and all the other articles contained in previous editions have been revised and brought up to date. There are a few chapters which may be open to some criticism. For example, the article on epilepsy, written by Pierce Clark, presents the author's well-known views that the convulsion is a defense reaction by which the patient retreats to a state of harmony and peace. This can scarcely be regarded as representative of neurological opinion. The old article by Southard on encephalitis has not been revised with sufficient care and is very confusing. Recent work in Germany on the nervous lesions following acute infectious diseases and on the so-called encephalitis congenita and other infantile brain lesions has done much to clarify the situation. Exception might also be taken to the haphazard arrangement which treats astasia abasia and adipositas dolorosa together and separates closely related subjects. There is also considerable overlapping.

These defects are minor ones, however, and there is really very little to criticise

in this volume. It stands as a substantial contribution to the study of clinical neurology and can be recommended to the student as an authoritative source of information.

F. R. F.

Fever, Heat Regulation, Climate, and the Thyroid-Adrenal Apparatus. By W. CRAMER. Pp. 153. 51 plates and figures. $6.00. (*Longmans, Green and Co., London, 1928.*)

All the factors concerned in the heat regulation of the body, with the exception of respiration, are considered by the author to be under direct control of the sympathetic nervous system, and therefore subject to control by the thyroid and adrenal glands. Exposure to cold increases, and to heat decreases, thyroid and adrenal activity; "bracing" and "relaxing" climates are also likewise considered to have opposing influences on these glandular secretions.

Dr. Cramer constructs his thesis mainly upon his own experimental data derived from histochemical (osmic acid vapor) methods, which are said to furnish directly conclusive evidence concerning glandular secretion. In the rat it would appear that fairly definite secretory changes may be observed; the glandular changes in the mouse, however, are admittedly not precise, although a good deal of the evidence has been derived from experiments on the latter animal. The numerous diagrams and pictographic summaries which are given would indicate that the observations and also the physiological conditions are delightfully clean-cut; but (perhaps fortunately) the normal activities in the body cannot, in the light of other research, be so simply considered.

A middle course is steered by the author in the decade-old controversy which has been waged mostly in this country on the functions of the adrenal medulla. Much of the work which has been done in the past few years on these functions is, however, not mentioned, although the book appears under date of 1928.

An argument on the "glycogenic function" (defined as "the internal secretion") of the liver occupies a considerable part of the volume. Mechanisms of inhibition and "self-control" in the adrenal gland are also dilated upon; the latter appears, it may be said, to be bringing the ego rather overmuch to the fore. Exophthalmic goitre is referred to as a breakdown in adrenal self-control.

The book contains a number of excellent half-tone reproductions, and somewhat less than two hundred references.

S. W. B.

The Physiology and Biochemistry of Bacteria. By R. E. BUCHANAN and E. L. FULMER. Vol. 1. pp. 516. $7.50. (*The Williams & Wilkins Co. Baltimore, 1928.*)

This volume contains the material presented to university students by two authorities, one on bacterial taxonomy and physiology, the other on biophysical chemistry. It begins with a section on methods of counting bacteria, bacterial

growth phases and rates, and a discussion of the theories and mathematics of these phenomena. The second section concerns itself with the chemical composition of bacterial cells and is fairly exhaustive, dealing with determinations of water, ash, inorganic constituents, proteins, fats, carbohydrates, etc., and their relation to the life and activities of the cells. The third section is chiefly an introduction to the fundamentals of Physical Chemistry. The last section deals with energetics and thermodynamic aspects of bacterial life. The book is well indexed as to authors, subjects and bacterial names.

The senior author has long interested himself in the general subject and especially in certain aspects of it, as in the growth phases of bacterial cultures and the thermodynamic features. Strictly speaking, however, comparatively little new material is presented. Much, except the first section, and a few pages in the last section can be found in up to date textbooks on physics and physical chemistry and such treatises as Bayliss' Physiology, Clark's and Michaelis' works on hydrogen ions and Hatschek's work on colloidal chemistry. But the selection and easy presentation of suitable material from the enormous mass available is a work and contribution for which every student and every newcomer into the field of bacteriology should feel extremely grateful and of which he should avail himself. The bibliography of nearly seven hundred references dating from about 1870 to 1927 makes this apparent.

The treatment is, in places, largely mathematical. Sometimes certain details are dwelt upon at perhaps disproportionate length as in the growth phase section and in one or two other places, giving evidence, it may be, of the authors' interest in these details. Certain other sections appear to have been rather casually treated.

In general, the book appears to be more of a treatise on physical chemistry and elementary thermodynamics with an occasional rather brief mention of the relation of these subjects to bacteriology. It gives a view of certain problems in biology from the standpoint of the physical chemist, arranged for the undergraduate student and useful also to the beginning research worker.

Biologists, (excepting professional biometricians), are seldom skilful mathematicians. Many, owing to the necessity for extreme specialization, find it difficult or impossible to keep abreast with developments in physics and chemistry which might help them to solve their problems in terms of the more exact sciences. It is for this reason that a treatise of the sort under discussion should be welcome to workers in all fields—not because it announces new theories and discoveries, but because it is a bridge over the all too wide gulf between the biologist, the physical chemist and the mathematician.

M. F., Jr.

The Management of the Sick Infant. By Langly Porter and W. E. Carter. 3rd revised edition. 8°. 726 pp. $8.50. (*C. V. Mosby Co., St. Louis, 1927.*)

Although the practice of Pediatrics in children over two years of age is closely akin to adult medicine, in the management of those under two there are many

features which are quite different. These differences the authors have duly emphasized. The volume is primarily a clinical work, giving a rather brief pointed description of the diseases themselves but with special emphasis on the actual bedside treatment. The last section is devoted entirely to a discussion of technique and methods which in many cases are applicable to actual treatment in the home.

As the title suggests, therapy is the chief concern of the authors and throughout the work, while not forgetting the scientific side, they have dealt with the bedside treatment in a way that must infallibly prove helpful to those who encounter in their practice the many puzzling problems presented by sick children.

E. M. B.

A Text-Book of Surgery. By W. WAYNE BABCOCK. 1367 pp. $10.00. (*W. B. Saunders Company, Philadelphia, 1928.*)

This is a new textbook of surgery. In his preface the author admits that he attempts a standardization of surgical knowledge. He frankly offers this as a student's book for students and it is with this end in view that everything is laid down in one, two, three order and in a thus and so manner. It is divided into four parts, general surgery, surgery of the systems, surgical technique, and regional surgery.

The many illustrations by McNett are excellent and help tremendously.

It is not a reference book; it has no bibliography and has but scanty hints in regard to medical history. All in all, it is a rather fair book for those who have just commenced the study of surgery.

W. M. M.

Nutrition. By WALTER H. EDDY. pp. 237. $2.50. (*The Williams & Wilkins Co., Baltimore, 1928.*)

This little book reflects, as is not unnatural, the particular interest of its author. Out of a total of 220 pages of reading matter just about one-half are devoted to the vitamins. This would seem either to be over-emphasis on this single topic or else the book has a rather poor title. The science of nutrition consists of a great deal more than vitamins. Just why the vitamins have taken such a hold on the popular imagination is no doubt due at least in part to the fact that they possess the glamour of mystery, and that they have had the overwhelming advantage of widespread publicity.

As is true of not a few of the current texts written by persons without unprejudiced clinical background, a good deal is taken for granted regarding the occurrence of vitamin deficiencies and their clinical significance. One can only agree with a recent article in the *Lancet* that, while the idea that body immunity is lowered by dietary deficiencies is an attractive one, it is remarkable how little experimental evidence there is in favor of it. Most of the statements which have

been published regarding the fertility vitamin, Vitamin E, seem to be accepted whole-heartedly by the author.

On the whole, the book is written in a most attractive style for the non-technical reader. It will have a purely popular appeal. Many of the statements it contains are generally accepted and found in every textbook; a few are open to question, and quite a few will certainly need revision if the author is so fortunate as to be compelled to issue future editions.

G. A. H., Jr.

The Elements of the Science of Nutrition. By Graham Lusk. Fourth Edition. 844 pp. 8°. $7.00. (*W. B. Saunders Co., Philadelphia, 1928.*)

The appearance of a fourth edition of this standard work is very welcome and all students will be glad that Professor Lusk has reconsidered the decision published in the preface to the last previous edition that he would not again revise it. At that time he stated that the next formulation of the subject would be from the standpoint of physical chemistry, but now he feels that the time for such a formulation has not yet arrived. Some will be inclined to query whether this time will arrive at all, at least for those now living, or why the need for a formulation from the standpoint of any particular discipline. Some time ago because of the wonderful advances in the field of cellular pathology, many felt that this science would explain everything or nearly everything of any importance. Organic chemistry, bacteriology and the science of immunity have also had their day. And now signs are not wanting that the rôle of physical chemistry in the biological sciences will become better defined shortly, that it will as well be shorn of many of its mysteries for the common man, and that it also will become one of a group of tools in the solution of biological problems, neither more nor less important than the rest.

A number of important alterations have been made in this edition. The author's peculiar ability to condense rather complicated material into a brief space without losing thereby important essentials or clarity is again strikingly shown. The chapter on oxidation and reduction is a good illustration of this ability. The exposition of the Hill-Meyerhof Theory of the energy production in muscular contraction in Chapter XVII, and the summary of present knowledge of the vitamins in Chapter XIX are others. The chapters on diabetes, clinical and experimental, have been thoroughly revised and bring their subject matter up to date. Certain other chapters may not seem so complete, particularly those dealing with clinical conditions. The one dealing with cardiac disease and nephritis is a case in point. The chapter on anemia and metabolism in high altitudes is good, but opinions may differ regarding some of the conclusions which are drawn and regarding the omission of work which seems important. All in all, there is no other book like this one in English and its value seems to increase with each succeeding revision.

G. A. H., Jr.

Max von Pettenkofer. His Theory of the Etiology of Cholera, Typhoid Fever and Other Intestinal Diseases. A Review of His Arguments and Evidence. By EDGAR ERSKINE HUME, Major, Medical Corps, U. S. Army. pp. 142. 8°. $1.50. (*Paul B. Hoeber, Inc., New York, 1927.*)

In this little publication of 142 pages, representing the thesis presented by the author for the degree of Doctor of Public Health in the School of Hygiene and Public Health of the Johns Hopkins University, Dr. Hume has given a brief account of von Pettenkofer's life and a comprehensive picture of his achievements. Coming as it does at the present time, when von Pettenkofer's work is constantly being judged by standards of knowledge obtained since his time as to the etiology and spread of disease, with an inevitable belittling of his achievements, this thesis will serve to restore to us a true appreciation of this great Bavarian savant. For it must be remembered that von Pettenkofer was one of the greatest and, in the opinion of some authorities, the greatest medical man of Germany in the last century. Indeed von Pettenkofer's conception of hygiene and public health was probably broader than that of any of his contemporaries and followers, and he trained a remarkable group of men who established institutes of hygiene in the German and Austrian Universities modeled after the institute which he himself organized in the University of Munich. Many of von Pettenkofer's contributions are likely to be forgotten and Dr. Hume has discovered a number which are seldom mentioned, such as his method of restoring the oil paintings whch were being injured and destroyed in the art galleries of Munich. The injury was done by the growth of mildews which made the varnish opaque and obscured the paintings. Von Pettenkofer made a chemical study of the oils and pigments used by the artists, found that the oil in which the pigments were dissolved took up oxygen from the atmosphere, with a condensation of water vapor on the surface and a subsequent cracking of the varnish. By the application of hot alcohol vapor the cracked varnish fragments were united and made translucent, the painting being thus made clear. This method came into general use and has proved of the greatest value in the preservation of the art treasures of Europe.

Von Pettenkofer's main positive contributions to hygiene and public health, such as his studies in respiration, ventilation and metabolism, are discussed by Dr. Hume clearly but somewhat too briefly for their importance. His investigations on the etiology and epidemiology of Asiatic cholera, typhoid fever and other intestinal diseases, regarded by von Pettenkofer as diseases of the soil (Bodenkrankheiten), are carefully presented, with a just appreciation of von Pettenkofer's difficulties but also of his tendency to make observations of his own and of others fit into his theories, and not to make his theories fit into observed facts. Finally, Dr. Hume has prepared an excellent bibliography of von Pettenkofer's publicatons, either by himself alone or with collaborators, which reaches the astonishing total of 227 papers in a period of 56 years, from 1842 to 1898. For all students of medicine in its broader aspects and for students interested in hygiene and public health especially Dr. Hume's book will prove of great interest and value. One

only wishes that the author had presented von Pettenkofer's life and work much more elaborately since he evidently had in hand the proper material for more than this brief publication.

W. W. F.

Blood. A Study in General Physiology. By LAWRENCE J. HENDERSON. 397 pp. $5.00. (*Yale University Press, New Haven, 1928.*)

Professor Henderson's work of the past decade is here discussed, amplified and summarized in its bearing on fundamental concepts in general physiology. Simplifying assumptions permit a roughly approximate definition of the blood as a physico-chemical system of two phases, cells and plasma, and eight principal components, H_2O, CO_2, O_2, HCl and other acids, plasma bases, cell bases, plasma protein and hemoglobin. These variables exist in a state of interdependence, and a description of this system is possible only by mathematical means. A nomographical synthesis of the known partial activities permits the description of the conditions of the stationary state (so-called equilibrium) in a sample of blood. As a result, it becomes possible not only to take account of the quantitative relations between the blood and the respiration and circulation during rest and work, in health and disease and from species to species, but also to describe the mutual dependence of the properties of blood and those of the circulation, respiration and metabolism.

Students of physiology will welcome the appearance of this volume. To those who view the onrushing flood of contemporary fact-collecting with justifiable dismay, Professor Henderson's attempt at integration of an important section of general physiology indicates a hopeful method of defense from apparently inevitable inundation.

B. C.

The Psychology of Mental Disorders. By ABRAHAM MYERSON, M.D. 135 pp. $1.40. (*The Macmillan Company, New York, 1927.*)

This book is written with the purpose of educating the public to dispel popular ignorance regarding mental disorders. The author primarily deals with facts although some theories are included. He begins with a discussion of the mind and defines it in an "organistic" sense as an expression of the whole personality, "interacting" with the physiological organism and the environment, a concept for which the term "integration" would be more acceptable to some readers. He then discusses the major mental disorders, with their outspoken symptoms and known and possible causes, giving another chapter to the minor mental diseases. He believes in calling a spade a spade, and has no patience with the tendency to obscure the latter under the name of "nervousness." Concerning those mental reactions of which the etiology is still debatable and speculative, the author discusses heredity and constitutional make-up, but leans toward the more optimistic view that many tendencies can be corrected by environment. Following

the chapter on the minor mental diseases, for the treatment of which he depends more on habit training, the author reviews Freud's theories with an open-minded attitude and with the criticism that they lack sufficient scientific control and should be tried out with the normal child. He leaves to time the question of Freud's lasting contribution to the study and cure of mental disease and gives him full credit for his permanent contribution to human thought and towards a closer achievement of a reasonable social scheme, free from prejudice and taboo regarding sex. The author discusses criminology and feeble-mindedness from his own experience, with special emphasis on the fact that the majority of these individuals do not profit through experience, and believes that after they become repeated offenders they may need permanent segregation. He makes a plea for more teaching and training to a purpose, the elimination of the street-corner gang and better entertainment as measures for prevention of crime. In the final chapter he urges more individual attention to the child, with especial emphasis on training in "strength, courage and endurance" as well as on the need of punishment and reward. The author's own sense of humor and fundamental common sense, for both of which he makes a special plea, make his book very readable.

R. E. F.

The Genesis of Epidemics and The Natural History of Disease. By CLIFFORD ALLCHIN GILL. 550 pp. $7.50. (*William Wood and Company, New York, 1928.*

The author presents an exhaustive treatise on the biological factors which cause disease to break out in epidemic form. To explain the periodicity of epidemics he presents a basic theory which he calls "The Quantum Theory" or the periodic loss of equilibrium between infection and immunity. In other words, when the population immunity is low, an epidemic will occur as soon as conditions favorable to transmission develop.

A large part of the book is devoted to the natural history of malaria, influenza and plague, and contains contributions from the author's experiences in India which should prove a valuable source of material to those interested in these diseases.

The book is an important contribution to science and is recommended not only to health officers but to others interested in natural science.

V. L. E.

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